RACT-00200 PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FIRST NAMED INVENTOR: MCDANIEL, C. STEVEN § DOCKET NO. RACT-00200
§
SERIAL NO.: 10/655,345 § GROUP ART UNIT: UNKNOWN
§
FILED: September 4, 2003 § EXAMINER: UNKNOWN
§
TITLE: BIOLOGICAL ACTIVE COATING COMPONENTS, COATINGS, AND COATED SURFACES §
§
§

Certificate of Mailing
I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope address Mail Stop Petitions, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on
11/11/03
Signature

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Petition Under 37 C.F.R. §§ 1.102(d) and 1.102(c) for Advancement of Examination of U.S. Patent Application No. 10/655,345, filed September 4, 2003

The Commissioner of Patents and Trademarks is petitioned in the first instance to make the above-identified application special under the provisions of 37 C.F.R. § 1.102(d) on the grounds that the claimed invention is a counter-terrorism invention.

Chemical weapon nerve agents include organophosphorus compounds such as sarin, cyclosarin, tabun, soman, and VX agent may be used in a terrorist act as defined under 18 U.S.C. 2331. These nerve agents are extremely toxic and may enter the body through inhalation, contact to the skin, or ingestion of contaminated food or drink. Sarin is a nerve agent that was used as a weapon of terror to kill 19 and injure approximately 6,000 people in Japan during 1994 and 1995. In addition, there is considerable concern that sarin or the more toxic nerve agents, such as soman and VX, may be obtained by terrorists and used domestically (see Exhibit A).

Among the various embodiments of the claimed invention is a coating, such as a paint, that comprises a biomolecule composition comprising an enzyme that can destroy these nerve agents (see Exhibit B: Preliminary Amendment U.S. Patent Application no. 10/655,345). This invention functions as a counter-terrorism invention as it can destroy nerve agents at the site of a terrorist attack, such as in buildings and vehicles. The invention can detoxify a contaminated surface (*e.g.*, a wall, a door, a floor, furniture, *etc.*) where people may contact the nerve agent. For example, a nerve agent destroying paint of the invention can be applied to the surface prior to an attack, and thus would be in position to begin immediate destruction of a nerve agent that contaminates the

surface. The ability of such a coating of the present invention to detoxify soman nerve agent on a surface is demonstrated at Example 6 of the above cited application, and is included herein as Exhibit C. In an additional example, a nerve agent destroying coating of the claimed invention may be applied to a surface after a nerve agent attack to decontaminate the surface.

The Commissioner is further petitioned in the second instance to make the above-identified application special under the provisions of 37 C.F.R. § 1.102(c) that the claimed invention can materially enhance the quality of the environment.

Various embodiments of the claimed invention can be used to destroy organophosphorus pesticides, which are similar to organophosphorus chemical warfare agents. Such compounds affect humans by the same mechanisms as such chemical warfare agents, but generally require many times the dosage to achieve lethality. However, organophosphorus pesticides are capable of producing ill-health effects in humans, and it has been estimated that organophosphorus pesticides accidentally poison thousands of persons each year (see Exhibit D, page 4). This invention can contribute to the restoration or maintenance of water and soil by its use to coat surfaces at sites where organophosphorus pesticides are released into the environment, such as in chemical plants, on farm equipment, or upon buildings used in agricultural functions. By such use, the compositions of the invention can destroy excess organophosphorus pesticides and reduce their undesirable spread beyond the specific site of use. Additionally, in the event of a spill of an organophosphorus pesticide, the compositions of the invention may be used to detoxify surfaces at the site of the spill, and thus reduce environmental contamination.

This petition is accompanied by the petition fee specified under 37 CFR 1.17(h). If any additional fee is required, the Office is requested to debit U.S.P.T.O. Account No. 50-1085 for such fees.

Respectfully Submitted,

MCDANIEL & ASSOCIATES, P.C.

By_____

C. Steven McDaniel
Attorney for Applicant
Reg. No. 33,962
Tel.: (512) 472-8282

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
McDaniel, C. Steven

Serial No. 10/655,345

Filed: September 4, 2003

For: Biological Active Coating Components, Coatings, and Coated Surfaces

Atty. Dkt. No.: RACT-00200

Examiner: Not Assigned

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail with sufficient postage in an envelope addressed to: Mail Stop Petitions, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on:

11/11/03 Renetta DeVeaux
Date **Signature**

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Transmittal Letter

Dear Sir:

Enclosed are the following:

1. Petition Under 37 C.F.R. §§ 1.102(d) and 1.102(c) for Advancement of Examination;
2. A Petition Fee specified under 37 CFR 1.17(h); and
3. Acknowledgment Postcard.

If any additional fee is required, the Office is requested to debit Deposit Account No. 50-1085 for such fees.

Respectfully submitted,

Date: 11.07.03

C. Steven McDaniel
Registration No. 33,962

McDaniel & Associates, P.C.
P.O. Box 2244
Austin, Texas 78768-2244
(512) 472-8282

EXHIBIT A

The risk of chemical and biological terrorism : discussing chemical disarmament in relation with the risk

Armand LATTES

Laboratoire des I.M.R.C.P. – UMR 5623
Université Paul Sabatier – 31062 TOULOUSE Cedex - France

Biological and chemical terrorism : fiction and reality

Biological and chemical terrorism are the use of biological and chemical agents to cause disease or death in man, animals and plants. With the end of the cold war, lobbyists, consultants and defense experts have moved their attention to exploring other possible threats. Although some people think is fiction recent events show it is reality : both biological and chemical agents in the hands of terrorists can be very deadly weapons.

The Aum Shinrikyo attacks in june 1994, in Matsumoto, Japan, which killed 7 and injured 500, and on the subway in Tokyo in march 1995, which killed 12 and injured 5500, were the first instances of large-scale terrorist use of chemical agents.

"Sarin in the subway"

On March 20 1995, thousands of commuters on their way toward on central Tokyo were gassed during a terrorist attack by a weird religious cult. They were on the subway train and many were napping on their way to work. A man, wearing sunglasses, got off the train before it reached its destination, and wait, leaving a package near the door. A clear liquid was seeping from it, and many people near enough began feeling dizzy and were bleeding from the nose and mouth.

Four similar incidents took place at about the same time in the Tokyo subway system. The packages were disguised to look like lunch boxes or soda containers, and it was reported that the clear liquid was on impure or dilute solution of Sarin, a nerve agent developed by nazy in Germany during the 1930's.

This was the beginning of a frightening future. For the modern world "organized and indiscriminate murder" on a large scale is clearly possible and chemical weapons are likely to be a terrorist's vehicle for mass destruction.

"chemical or biological weapons ?"

Aum Shinri kyo was also experimenting with biological agents :

- police were reported to have confiscated 200 large containers of a solution used to cultivate bacteria and other micro-organisms as well as quantities of botulinus toxin ;
- the terrorist group sought to obtain Ebola virus

- and made at least nine attempts to aerosolize anthrax and bolulism throughout Central Tokyo : **without results** ! It is one of the reasons of the difficulty to use biological weapons : their impredictability, given their capacity to be affected by environmental conditions. However, Aum's leader, Shoko Asahara, remained enamored with BW, and it turned to CW only because it failed repeatedly to produce biological weapons.

Is CB terrorism an isolated phenomenon ?

There is sufficient evidence in the public domain to indicate that terrorist groups have indeed displayed in acquiring chemical agents and in some cases actually succeeded in attempts to make use of them. A variety of incidents and reports over the last years show interest in these weapons. For example :

- in february 1996, german police confiscated from a neo nazi group a codded diskette that contained information on how to produce the chemical agent mustard gas ;
- in january 1995, tajik opposition members at a new years celebration laced champagne with cyanide killing 7 people and sickening other revelers ;
- the PKK (Kurdistan's worker party), in southest Turkey, poisoned Turkisk water supplies with cyanide. etc...etc...etc...

The chief advantage of CB weapons are :

- the unrestricted availability of the necessary informations ;
- the (relatively) small resources needed ;
- the ability to test the product ;
- their production under the cover of an apparently legitimate commercial venture.

The terrorism at the plant level

In my opinion, one of the most important risk is "the terrorism at the plant level". In the days following the september 11 terrorist attacks, chemical plant U.S. officials say they have increased security through greater plant surveillance. The chemical industry understands the risk ! Recently greenpeace posted a map on its website showing the distance that chemicals could travel from a facility during a worst-case accident scenario. From (approximatively) Baton Rouge to New Orleans, 40 to 50 miles diameters circles can be drawn, each circle representing a chemical plant along the Mississipi River !

Last 21 sept., in Toulouse, France, 300 tons of ammonium nitrate have exploded killing 30 people ; 5500 were injured and nearly 20 000 houses or apartments were totally or partially destroyed. At this time we don't know the reason of this explosion, but the impact of this event was very important and, it seems to me, it is a good illustration of this risk.

Chemical weapons agents

There are literally ten of thousands of highly poisonous chemicals. It may not necessarily even include the use of weapons as such against a military target. Many toxic chemicals in wide use in the global chemical undustry, if used as a weapon on unprotected

civilians, may be as devastating as the use of CW designed to inflict damage and casualties on protected groups.

It is the case of commercially available **pesticides**, for example :

- insecticides, such as parathion, and TEPP (TEPP is the most toxic of the commercially available insecticide !)
- herbicides, such as TCDD (dioxin).

There are four major categories of substances affecting humans previously used as CW in different conflicts :

1 – Blistering agents

These substances are intended to cause incapacitation rather than death. Their use by a terrorist group depends largely on the groups objectives and moral standing. If their intention is to injure many people while causing as few deaths as possible, then a blister agent such as *Lewisite* or *mustard gas* may be the best choice. Abandoned old chemical munitions of the world war I have been stored in less than ideal conditions for the past 80 years and terrorists might get access to these substances, but the gas recovery from the munitions is difficult.

2 – Choking agents

These substances are intended to cause death and offer their greatest advantage to terrorist by being easily obtained. *Phosgene* (CG) is the most known of these agents : it is a common industrial chemical with a moderate lethal dose.

3 – *Blood agents* such as cyanide base compounds (e.g. hydrogen cyanide (AC). These compounds are not really suited for use on large numbers of people, they are essentially useful in assassinations.

formulas for manufacturing all these agents are readily available in various scientific texts.

4 – *Nerve agents such as* :
- tabun (GA) (the easiest to make) ;
- sarin (GB) the most effective ;
- VX ;
- soman (GD) ;
- Novichok (new class of lethal nerve agents from NUKUS, UZBEKISTAN) they are hundreds to thousands of times more lethal than precedent agents.

They are the likeliest weapons of choice for terrorists, given their lethality : they can be synthesized by a moderately competent organic chemist, with limited laboratory facilities.

How to acquire chemical agents ?

Some terrorist groups are capable to manufacture chemical agents on its own. Others ways to acquire chemical agents are :

1. direct use of commercially available poisons ; CW are relatively easy to purchase on the black market, particularly since they were so widely deployed during the IRAN-IRAQ war in the 1980's ;
2. the theft of chemical munitions held by the military.

In 1982, the U.S government has acknowledged that a small amount of its inventory of VX was presently unaccounted for. There have been known instances of its being rather casually offered for sale in New York city.

Five years before, the U.S. army announced that it planned to dispose of several batches of obsolete chemical warfare agents, some of them lethal... Two of the facilities which the army conveniently listed and the media made public were : the Brooklyn army Base and the Freeport Naval Reserve Center on Long Island... and **"these facilities had less security than a local supermarket"**.

Until, 2001 september 11, the 1623 one-ton cylinders of liquid mustard gas stocked neatly in an open field in Maryland, covered only by empty cylinders and enclosed within two chain link fences, offered terrorists a tantalizing target ! (The army has since tightened security, has sent in hundreds of troops to guard the perimeters, and has imposed no flight-zone over the site).

3. the receipt of ready-made chemical weapons from a state sponsor.

The US congressional office of technology assessment notes the ability to Libya, Iran and Iraq to produce CW together with the fact that all these countries have sponsored active terrorist groups that have attacked civilian population.

How to deliver CB agents ?

The effective dissemination or delivery of CB agents by terrorists is more difficult than their production or acquisition. In the past incidents it has typically been very simple in design or procedure, and of corresponding low efficiency. Possible methods include :

1- *Contamination of foodstupp or liquids*, e.g. at a water reservoir or at a bottling plant ; 43 % of the past incidents of CB terrorism (over 200 !) have been blamed to contaminated food and drink, 13 % on contaminated consumable products and 12 % on water supplies.

Remark : - The most popular scenario of poisoning a city's water supply is dumping something into a reservoirs, but :

- major reservoirs hold anything from a few months to a ten years supply with supplementation by ground water infiltration and well pumping
- a great quantity of water drawn from an urban supply never comes into physical contact with the population (water lawns, washes clothes and cars, flushes toilets, cools inudstrial equipment, etc...).

For example, it has been calculated that for a reservoir which is the sole source of water for a community of 10 000 and holds only a two years supply, if each member of the community drinks one liter of water a day :

- 7 billion lethal dose would be needed in the reservoir to deliver one dose per victim or, to be more specific : 7 tons to 7000 tons of chemical agents, 700 g to 7 tons of toxin agents (7 kg of pure BTX toxin) 300 tons of 8-fluorooctanol (the most stable chemical poison) !

2. *dispersal as vapour or via aerosol*, using a truck-mounted dispenser or an aircraft operating in a crop-duster fashion (9 % of the past incidents).
Aum's sect has used truck equipped with a commercial aerosolizer such as to spray trees and plants, around the government building : without results !

3. *contaminated personal items* –e.g. clothing) or direct human contact as in the case of the ricin-tipped umbrellas used in various assassination attempts (4% of the past incidents)

4. *explosive dispersal*, but with a significant loss of agents (3 %) etc... etc...

What are the best targets for terrorists ?

All authors agree that a smaller-scale attack confined to an enclosed area, but still capable of causing massive casualties, would be the best targets for terrorists, for example :
shopping malls, embassies, military facilities, convention centers, domed sports stadium, sealed building with central air conditioning, convention centers, subways, etc...

What about financing weapons acquisition by terrorists ?

Well executed, mass terror with chemical or biological agent would be very expensive. Moreover, restricting chemicals used to make chemical warfare agents or used as CW agents merely increases the costs for a group to obtain their weapons.

For this reason, we have to pay special attention to the link between terrorists and criminal organizations engaged in drug-trafficking, money-laundering or others illicit traffics. It is the same for the activites of different ethnic and religious foundations that may combine their social activity with the support of terrorists.

Why the chemical disarmament is able to diminsh the terrorism risk ?

The most effective deterrent to the threat of chemoterrorism is to deny terrorist access to these weapons and the chemicals needed for their production.

Approximatively 26 states have developped a CW arsenal ; with the huge quantities of chemical governments have produced for combat usage :
30.000 tons in U.S.A.
40.000 tons in Russian federation
(and, may be, 40.000 tons in IRAQ) terrorists could steal chemical agents.

Most of these chemical agents are in storage facilities. Comparing nuclear facilities, biological research laboratories, the chemical agent storage sites would be easiest to penetrate. All that would be necessary to recover the chemical agents would be for the terrorists to locate a disposal site and go retrieve the chemical agent.

In today's Russia, supertoxic agents are stored at seven depots throughout the country where securtiy measures are poor and could be penetrated by terrorists. Russian chemical munitions are in good conditions and have excellent agent-dispersal ability : only destruction of the weapons will remove the threat.

About fighting the proliferation of CB weapons, it is also necessary to provide sufficient resources to enable brain-drain prevention funding to reach the large community of russian weaponeers.

Moreover there is the possiblity for rogue states to supply chemical weapons to terrorists groups

"CHEMICAL ATTACKS BY TERRORISTS WILL ALMOST CERTAINLY BE DRIVEN BY THE PROLIFERATION OF CHEMICAL ARSENALS AMONG THEIR STATE SPONSORS"

In all cases there is a close connection between international terrorism and the illegal movement of potentially deadly materials.

Individual member states must take national steps to eliminate this danger, but states must also work in concert : the Chemical Weapons Convention (CWC) is an international control agreement helping to contain the threat of chemical terrorism.

Chemical Weapons Conventions (CWC)

On 13 january 1993, CWC was opened for signature in Paris : over to day it was signed by 143 states.

Implementation of the CWC is based on a regime of declaration and a regime of verification

1) for the chemical industry : declarations and verifications of declarations by on-site inspections ;
2) for chemical weapons and associated facilities : declaration and verification of destruction.

With the CWC, an Organization for the Prohibition of Chemical Weapons (OPCW), has been established to oversee the implementation of the CWC at international level, particularly through verification measures.

The OPCW consists of three main organs :

1) Conference of the State Parties ;
2) Executive council ;

3) Technical secretariat ; it provides all support to the CWC and also receives and then verifies the declarations sent to it by member states, and carries out the inspections specified in the Convention.

Toxic chemicals and their precursors are classified in three Schedules :

Schedule 1 : contains military agents and super toxic chemicals with very limited commercial use (mustard gas...)

Schedule 2 : chemicals have low to moderate utility in the commercial sector, but they can be used as chemical weapons or are precursors of chemical weapons (pesticides...)

Schedule 3 : chemicals are used in large quantities by commercial industry, but they have been used as CW or precursor (phosgene...).

Other **Discrete Organic Chemicals** are not included on there Schedules, but are subject to verification (organic chemicals containing the elements : phosphorus, sulfur or fluorine).

Challenge inspections

Any international reponse to prevent chemoterrorism hinges on the ability to restrict production of CW. The first article of the CWC specifies :

"all states parties will, within a period of 10 years, destroy the chemical weapons held on their territory or abandoned on the territory of another State Party, together with the destruction of any chemical weapons production facilities".

The most powerful instrument that has ever been placed in any multilateral disarmament treaty is the **challenge inspections** which in case of concern about compliance, can be requested by any state party against any facility or site in any other state party.

"Those inspections are conducted with a 12-hour notice"

To now a large number of inspections have been conducted in more than 50 countries around the world. As an example of such inspections it was the first US inspection of a chemical arms depot.

Less than 2 months after the CW treaty went into effect, the US was notified that its RICHMON, Ky., chemical weapons storage site would be inspected by an international team from the OPCW.

The inspection began 5 days after OPCW notified the US that the weapons storage facility (Blue grass) had been selected for a routine inspection (there were 70.000 nerve gas rockets and 30.000 mustard gas artillery shells). By all accounts, the inspection went "very, very well".!

Entry into force of the CWC and related problems

The CWC entered into force on 29 april 1997. Nevertheless there were, **and there are**, many problems, essentially :

- legal
- environmental and societal,
- and technical.

Legal :

In US and Russia, the vote for ratification of the CWC came after years of delay ! In USA, the vote came after several months of very intense public discussion and 2 full days of senate floor debate on the treaty. Much of this contentious discourse concerned the scientific and technical aspects of the pact.

On 24 april 1997, the US ratified the CWC. Five days later the treaty took effect. A month later, the US was technically out of compliance. Why ?

- Instead of sending a complete declaration to the OPCW, the US sent 3 volumes tallying all military facilities and, essentially, a note saying the US has "about" 2000 commercial facilities that will eventually be reporting data ;

- Because the US as yet no legislation setting out the legal and regulatory framework for implementing the treaty, commercial companies did not have to supply information required for the first declaration ;
- one provision of the Senate bill exempts waste streams from being considered DOC producers

THE LACK OF INSPECTIONS AT COMMERCIAL FACILITIES IS EXPECTED TO HAVE DIRE CONSEQUENCES ON THE TREATY'S NON PROLIFERATION EFFORTS.

The US is not alone in being out of compliance. About half of the countries that have ratified the treaty have submitted initial declaration, and many of there are incomplete.

Some of the initial reports have been extremely interesting. India, for example, has declared a chemical stockpile that it had previously denied having !

Remark : **the Chemical Agent Identification Sets (CAIS)**

Tens of thousands of Chemical Agent Identification Sets (CAIS) that the U.S. Army used from 1928 to 1969 to train soldiers to defend themselves against chemical weapons attack, need to be destroyed. This problem is complicated by legal issue as well as technical, environmental and societal issues.

Most of the kits contain glass vials of small quantities of the blister agents sulfur mustard and lewisite ; they are classified as chemical warfare material : such a classification precludes their disposal at commercial hazardous waste facilities.

Moreover, because they are considered **non stockpile materiel**, the U.S. Army, by law, is not allowed to incinerate them at the eight U.S. installations slated to destroy the nation's arsenal of chemical weapons !

Before the destruction of the kits :

- the army would still have to get Congress to amend the law prohibiting the use of the eight stockpile destruction facilities from destroying materiel other than CW !
- the amount of business would be relatively small, new equipments would be necessary and few commercial firms may be willing to take on the business !

Environmental and societal issues

Public needs voice in Chemical Arms disposal ! For example in Russia. So far there is no legislative guaranteeing of the Russian Chemical Disarmament. At any rate there are no Federal laws that are acceptalbe for the population. The Russian Union for Chemical Safety was founded in 1993 by different people from Universities, associations, etc... They were fighting for the humanity of the federal law "about the cw's destruction for a year and a half, with two suggestions on the people's collective social rights : unfortunatelly, both their suggestions were thrown away by the state Duma deputies !

Moreover, the process of choosing places for CWs destruction (7 places at beginning, only 3 now) in, or near, the place of their present storage, is a controversial one with the inhabitants. They ask the Russian government to do the process of choosing places according to all the rules of normal attitude to people.

Another problem with Russia is **the cost of disarmament** ! Cash-strapped Russia has said it is unable to meet it commitment to destroy its 40.000 tons of CW by 2007. With help from other countries, Russia believes it can destroy 20 % of its stockpile by 2007 and all of its stocks by 2012. Russia had initially planned to build 7 destruction facilities but now plans to build only 3 ! This decision accompanies the design and construction of a pilot-nerve agent destruction plant at a weapons depot near SHCHUCHIE in the Kurgan region near Kazakhstan.

Nerve agent weapons would then be transported from other storage sites to the destruction plant of SHCHUCHIE and possibly another central location. Communities in Russia hope that this transport and CWs destruction are possible in a safe environmentally sound manner.

BEYOND THE SPECTER OF CHEMICAL TERRORISM, THESE SITUATION WILL HAVE OTHER NEGATIVE CONSEQUENCE FOR NATIONS SECURITY. IT WILL SERIOUSLY UNDERMINE THE CWC. UNABLE TO COMPLY WITH THE OBLIGATIONS TO DESTROY THE CHEMICAL STOCKPILE, RUSSIA MAY HAVE NO CHOICE BUT TO WITHDRAW FROM THE TREATY.

Technology, technical problems

Most of the destruction costs are generated by the need to have high technology to ensure that the risk to people and to the environment is kept to the minimum at every stage

in the transportation, preparation and opening of munitions as well as during the removal of chemical agents and their eventual destruction.

There are two main techno logical approaches to the destruction of chemical agents :

- the direct incineration of the agents,
- and their neutralization by means of various chemical reactions
  * hydrolysis of nerve agents (Phosphorus compounds)
  * oxidation of blister agents (sulfurous compounds)

In the United States the process of destroying the chemical weapons stockpiles is already going ahead. In fact it had started before the entry into force of the Convention.

At first, two dispersal facilities have been built :

- the Johnston Atoll Chemical Agent Disposal System (JACADS) in the Pacific Ocean ;
- the Tooele Chemical Agent Disposal Facility near Salt Lake City.

1. JOHNSTON ATOLL is a flyspeck, some 717 nautical miles southwest of Hawaï. It has not indigenous population and all factors made the atoll the choice site for a fully integrated incinerator destruction facility. It was opened in 1990 and, on sept. 29 2000, the Army had announced that it began to destroy 13,302 land mines filled with VX nerve agent after the destruction of 399,430 munitions containing the nerve gas GB, the blister agent HD (mustard gas) and these same agents, in bulk form. Then, after destroying 2031 tons of munitions, the Army has closed the JACADS site. Previously the U.S. stocks from germany have been destroyed by incineration in this atoll.

2. The TOOELE facility in UTAH contained the largest stocks of U.S. CW, its incinerator is expected to burn about 40 % of the total stockpile of US chemical weapons. If all goes well, TOOELE is slated to close down at the end of 2003.

Other US facilities are :

- Anniston army depot (Alabama)
- Pine Bluff arsenal (Arkansas)
- Umatilla army depot activity (Oregon)
- Pueblo army depot activity (Colorado)
- Lexington-Blue grass army depot (Kentucky)
- Newport army Ammunition plant (Indiana)
- Aberdeen Proving ground (Maryland)

incineration as well as chemical neutralization methods are developped in some of them. According to James L. BACON, program manager for chemical demilitarization, more than 86 % of the U.S. chemical stockpile "is now under contract for destruction".

The Russian Federation has indicated that it will need international assistance to meet the destruction time-lines. This cooperation is planned on CWC, and several state parties and organisation are already providing such assistance.

Nevertheless there is a specific problem with the destruction of extremely dangerous new class of lethal nerve agents (e.g. novichok) : up to date scientists have not the technologies !

Destruction of old and/or abandoned chemical weapons

Old and/or abandoned chemical munitions often require much more manual handling than chemical munitions produced relatively recently and there is a greater risk of an explosive detonation or agent contamination.

Unexploded chemical munitions continue to be found in European countries on former world war I battlefieds. Last year a city in the North of France, having 12,500 inhabitants was evacuated during 1 week because it was necessary to take off old munitions from a stockpile of the world war I.

It is turns out that the CW were in fact brought by one state party into the territory of another and abandoned there **after 1925**, the abandoning state must then accept responsibility for their destruction. So, the treaty commits Japan to cleaning up the hundreds of thousaunds of chemical munition it left behind in China in 1945 when it was routed from the country. Japan has agreed in principle to pay for the destruction of its abandoned chemical weapons.

Converting chemical arms plants to peaceful uses

DUPONT is investing $10 million in a joint venture with a Russian Company, A.O. KHIMPOM, NOVOCHEBOKJARSK, to build a herbicide production facility on a complex that once also housed a soviet union chemical weapons facility. The venture aims to serve Russia's rapidly expanding agricultural markets, which could reach $ 1 billion within a decade.

Chemical weapons were made on a highly secured part of the complex and that part would have to be destroyed or **converted to peaceful uses** under strict chemical weapons convention guidelines. Approval for conversions must come from the OPCW, to ensure that the converted facilities are no longer able to produce chemical weapons.

The U.S. government is now seeking OPCW approval for conversion of a declared chemical weapons production facility in Van Nuys, California.

Japan has asked OPCW to consider the maintenance of the site where the Aum sect made the Sarin it used in the Tokyo Subway, as trial evidence to be a peaceful conversion but in 1997 OPCW has denied that request.

By way of conclusion

The world community has shown little outrage at the use of CW by both IRAN and IRAQ in their war. Perhaps a psychological barrier has already been broken for terrorists to use them. The taboo against the use of CW seems to have worn off.

Despite to change the situation, the threat of CB weapons remains. Terrorists should be prevented either from producing or using CW as well as from acquiring and using hazardous chemicals as means of inflicting casualties.

Research and production facilities, in some countries, are poorly guarded and vulnerable : in 1997 a visit of one of Russia's largest and most sophisticated former bioweapons facilities called **Vector** found a half-empty facility protected by handul of guards who hat not been paid for months.

Former east-countries CB weapons specialists have received some US or European funding to redirect their research for peaceful purposes... But you can't rule out people engaging in proliferation through temptation on corruption.

High decontamination capacity is one of the factors which may reduce the effect of an attack with CW agents.

It is obvious that the lion's share of the work to protect against chemical terrorism lies with national governments, however we believe that international organization such as the OPCW do have a predominant role in reducing the risk. Unhappily there is not certainty about what happens in those countries which have not joined the CWC.

Disarmament and non proliferation programs are essential and the destruction of the CW stockpiles must be completed as quickly as possible : this is a task of utmost importance to make our world safe and stable.

EXHIBIT B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FIRST NAMED INVENTOR:	MCDANIEL, C. STEVEN	§	DOCKET NO. RACT-00200
SERIAL NO.:	10/655,345	§	GROUP ART UNIT: UNKNOWN
FILED:	September 4, 2003	§	EXAMINER: UNKNOWN

TITLE: BIOLOGICAL ACTIVE COATING COMPONENTS, COATINGS, AND COATED SURFACES §

Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope address to Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450 Washington, D.C. 22313-1450 on 10.23.03

Regretta DeVeau
Signature

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Washington, DC 22313-1450

Preliminary Amendment

Sir:

Please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims, which begins on page 2 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 2 (original): The coating of claim 1, wherein the active biomolecule comprises a proteinaceous molecule.

Claim 3 (original): The coating of claim 2, wherein the proteinaceous molecule binds a ligand, contacts a living organism, or a combination thereof.

Claim 4 (original): The coating of claim 3, wherein the proteinaceous molecule binds a ligand.

Claim 5 (original): The coating of claim 4, wherein the ligand comprises an antigen, a substrate, an inhibitor, or a combination thereof.

Claim 6 (currently amended): The coating of ~~claim 5~~ claim 4, wherein the ligand comprises a chemical toxic to humans.

Claim 7 (currently amended): The coating of ~~claim 6~~ claim 4, wherein the ligand comprises an organophosphorus compound.

Claim 8 (original): The coating of claim 2, wherein the proteinaceous molecule comprises a peptide, a polypeptide, a protein, or a combination thereof.

Claim 9 (currently amended): The coating of ~~claim 8~~ claim 2, wherein the proteinaceous molecule comprises an enzyme, an antibody, a receptor, a transport protein, structural protein, or a combination thereof.

Claim 10 (currently amended): The coating of ~~claim 8~~ claim 9, wherein the proteinaceous molecule comprises an enzyme.

Claim 11 (original): The coating of claim 10, wherein the enzyme comprises an oxidoreductase, a transferase, a hydrolase, a lyase, an isomerase, a ligase, or a combination thereof.

Claim 12 (original): The coating of claim 11, wherein the enzyme comprises a hydrolase.

Claim 13 (original): The coating of claim 12, wherein the hydrolase comprises an esterase.

Claim 14 (original): The coating of claim 13, wherein the esterase comprises a phosphoric triester hydrolase.

Claim 15 (original): The coating of claim 14, wherein the phosphoric triester hydrolase comprises an aryldialkylphosphatase, a diisopropyl-fluorophosphatase, or a combination thereof.

Claim 16 (original): The coating of claim 14, wherein the phosphoric triester hydrolase comprises a combination of phosphoric triester hydrolases.

Claim 17 (original): The coating of claim 15, wherein the phosphoric triester hydrolase comprises an aryldialkylphosphatase.

Claim 18 (currently amended): The coating of ~~claim 15~~ claim 17, wherein the aryldialkylphosphatase comprises an organophosphorus hydrolase, a human paraoxonase, an animal carboxylase, or a functional equivalent thereof.

Claim 19 (currently amended): The coating of ~~claim 15~~ claim 18, wherein the aryldialkylphosphatase comprises an organophosphorus hydrolase or a functional equivalent thereof.

Claim 20 (original): The coating of claim 19, wherein the organophosphorus hydrolase comprises an *Agrobacterium radiobacter* P230 organophosphate hydrolase, a *Flavobacterium balustinum* parathion hydrolase, a *Pseudomonas diminuta* phosphotriesterase, a *Flavobacterium sp opd* gene product, a *Flavobacterium sp.* parathion hydrolase *opd* gene product, or a functional equivalent thereof.

Claim 21 (original): The coating of claim 20, wherein the organophosphorus hydrolase comprises a functional equivalent of *Agrobacterium radiobacter* P230 organophosphate hydrolase, a *Flavobacterium balustinum* parathion hydrolase, a *Pseudomonas diminuta* phosphotriesterase, a *Flavobacterium sp opd* gene product, or a *Flavobacterium sp.* parathion hydrolase *opd* gene product.

Claim 22 (original): The coating of claim 21, wherein the functional equivalent is a structural analog.

Claim 23 (currently amended): The coating of claim 22, wherein the structural analog comprises a Co^{2+}, Fe^{2+}, Cu^{2+}, Mn^{2+}, ~~Cd^{2+}, or Ni^{2+}~~ Cd^{2+}, or Ni^{2+} at the enzyme active site.

Claim 24 (original): The coating of claim 21, wherein the functional equivalent is a sequence analog.

Claim 25 (currently amended): The coating of ~~claim 21~~ claim 24, wherein the sequence analog is an alteration in sequence length.

Claim 26 (original): The coating of claim 24, wherein the sequence analog lacks a leader peptide sequence.

Claim 27 (original): The coating of claim 24, wherein the sequence analog is a fusion protein.

Claim 28 (original): The coating of claim 20, wherein the organophosphorus hydrolase comprises a *Pseudomonas diminuta* phosphotriesterase, or a functional equivalent thereof.

Claim 29 (original): The coating of claim 28, wherein the organophosphorus hydrolase comprises a *Pseudomonas diminuta* phosphotriesterase.

Claim 30 (original): The coating of claim 28, wherein the organophosphorus hydrolase comprises a *Pseudomonas diminuta* phosphotriesterase functional equivalent.

Claim 31 (currently amended): The coating of ~~claim 28~~ claim 30, wherein the *Pseudomonas diminuta* phosphotriesterase functional equivalent comprises a sequence analog.

Claim 32 (original): The coating of claim 31, wherein the sequence analog comprises an amino acid substitution.

Claim 33 (original): The coating of claim 32, wherein the sequence analog is H55C, H57C, C59A, G60A, S61A, I106A, I106G, W131A, W131F, W131K, F132A, F132H, F132Y, L136Y, L140Y, H201C, H230C, H254A, H254R, H254S, H257A, H257L, H257Y, L271A, L271Y, L303A, F306A, F306E, F306H, F306K, F306Y, S308A, S308G, Y309A, M317A, M317H, M317K, M317R, H55C/H57C, H55C/H201C, H55C/H230C, H57C/H201C, H57C/H230C, A80V/S365P, I106A/F132A, I106A/S308A, I106G/F132G, I106G/S308G, F132Y/F306H, F132H/F306H, F132H/F306Y, F132Y/F306Y, F132A/S308A, F132G/S308G, L182S/V310A, H201C/H230C, H254R/H257L, H55C/H57C/H201C, H55C/H57C/H230C, H55C/H201C/H230C, I106A/F132A/H257Y, I106A/F132A/H257W, I106G/F132G/S308G, L130M/H257Y/I274N, H257Y/I274N/S365P, H55C/H57C/H201C/H230C, I106G/F132G/H257Y/S308G, or A14T/A80V/L185R/H257Y/I274N.

Claim 34 (currently amended): The coating of ~~claim 17~~ claim 18, wherein the aryldialkylphosphatase comprises a human paraoxonase or a functional equivalent thereof.

Claim 35 (original): The coating of claim 34, wherein the human paraoxonase comprises an HPON1 gene product or a functional equivalent thereof.

Claim 36 (original): The coating of claim 35, wherein the human paraoxonase comprises a HPON1 gene product functional equivalent.

Claim 37 (currently amended): The coating of ~~claim 28~~ claim 36, wherein the HPON1 gene product functional equivalent comprises a sequence analog.

Claim 38 (original): The coating of claim 37, wherein the sequence analog comprises an amino acid substitution.

Claim 39 (original): The coating of claim 38, wherein the sequence analog is E32A, E48A, E52A, D53A, D88A, D107A, H114N, D121A, H133N, H154N, H160N, W193A, W193F, W201A, W201F, H242N, H245N, H250N, W253A, W253F, D273A, W280A, W280F, H284N, or H347N.

Claim 40 (currently amended): The coating of ~~claim 17~~ claim 18, wherein the aryldialkylphosphatase comprises an animal carboxylase or a functional equivalent thereof.

Claim 41 (original): The coating of claim 40, wherein the animal carboxylase comprises an insect carboxylase or a functional equivalent thereof.

Claim 42 (currently amended): The coating of claim 41, wherein the insect carboxylase comprises a *Plodia interpunctella* carboxylase, *Chrysomya putoria* carboxylase, *Lucilia cuprina* carboxylase, *Musca domestica* carboxylase-~~carboxylase~~, or a functional equivalent thereof.

Claim 43 (original): The coating of claim 15, wherein the phosphoric triester hydrolase comprises a diisopropyl-fluorophosphatase.

Claim 44 (original): The coating of claim 43, wherein the diisopropyl-fluorophosphatase comprises an organophosphorus acid anhydrolase, a squid-type DFPase, a Mazur-type DFPase, or a functional equivalent thereof.

Claim 45 (original): The coating of claim 44, wherein the diisopropyl-fluorophosphatase comprises an organophosphorus acid anhydrolase or a functional equivalent thereof.

Claim 46 (original): The coating of claim 45, wherein the organophosphorus acid anhydrolase comprises an *Altermonas* organophosphorus acid anhydrolase, a prolidase, or a functional equivalent thereof.

Claim 47 (original): The coating of claim 46, wherein the organophosphorus acid anhydrolase comprises an *Altermonas* organophosphorus acid anhydrolase or a functional equivalent thereof.

Claim 48 (original): The coating of claim 47, wherein the *Altermonas* organophosphorus acid anhydrolase comprises an *Alteromonas* sp JD6.5 organophosphorus acid anhydrolase, an *Alteromonas haloplanktis* organophosphorus acid anhydrolase, an *Altermonas undina* organophosphorus acid anhydrolase, or a functional equivalent thereof.

Claim 49 (original): The coating of claim 46, wherein the organophosphorus acid anhydrolase comprises a prolidase or a functional equivalent thereof.

Claim 50 (original): The coating of claim 49, wherein the prolidase comprises a human prolidase, a *Mus musculus* prolidase, a *Lactobacillus helveticus* prolidase, an *Escherichia coli* prolidase, an *Escherichia coli* aminopeptidase P, or a functional equivalent thereof.

Claim 51 (original): The coating of claim 44, wherein the diisopropyl-fluorophosphatase comprises a squid-type DFPase, or a functional equivalent thereof.

Claim 52 (original): The coating of claim 51, wherein the squid-type DFPase comprises a *Loligo vulgaris* DFPase, a *Loligo pealei* DFPase, a *Loligo opalescens* DFPase, or a functional equivalent thereof.

Claim 53 (original): The coating of claim 52, wherein the squid-type DFPase comprises a *Loligo vulgaris* DFPase, or a functional equivalent thereof.

Claim 54 (currently amended): The coating of claim 53, wherein the squid-type DFPase comprises a *Loligo vulgaris* DFPase~~, or a functional equivalent thereof~~.

Claim 55 (currently amended): The coating of ~~claim 54~~ claim 53, wherein the squid-type DFPase comprises a *Loligo vulgaris* DFPase functional equivalent.

Claim 56 (original): The coating of claim 55, wherein the *Loligo vulgaris* DFPase functional equivalent comprises a sequence analog.

Claim 57 (original): The coating of claim 56, wherein the sequence analog comprises an amino acid substitution.

Claim 58 (original): The coating of claim 57, wherein the sequence analog is H181N, H224N, H274N, H219N, H248N, or H287N.

Claim 59 (currently amended): The coating of ~~claim 57~~ claim 56, wherein the sequence analog is an alteration in sequence length.

Claim 60 (original): The coating of claim 59, wherein the sequence analog is a fusion protein.

Claim 61 (original): The coating of claim 44, wherein the diisopropyl-fluorophosphatase comprises a Mazur-type DFPase or a functional equivalent thereof.

Claim 62 (original): The coating of claim 61, wherein the Mazur-type DFPase comprises a mouse liver DFPase, a hog kidney DFPase, a *Bacillus stearothermophilus* strain OT DFPase, an *Escherichia coli* DFPase, or a functional equivalent thereof.

Claim 63 (currently amended): The coating of ~~claim 1~~ claim 14, wherein the phosphoric triester hydrolase comprises a *Plesiomonas* sp. strain M6 *mpd* gene product, a *Xanthomonas sp.* phosphoric triester hydrolase, a *Tetrahymena* phosphoric triester hydrolase, an insect cholinesterase, or a functional equivalent thereof.

Claim 64 (currently amended): The coating of ~~claim 2~~ claim 3, wherein the proteinaceous molecule contacts a living organism.

Claim 65 (original): The coating of claim 64, wherein the proteinaceous molecule comprises a ligand capable of binding to an active biomolecule of the living organism.

Claim 66 (original): The coating of claim 65, wherein the active biomolecule of the living organism comprises a receptor, an enzyme, a transport protein, or a combination thereof.

Claim 67 (currently amended): The coating of claim 1, wherein the ~~biomolecular~~ biomolecule composition comprises 0.001% to 40% of the coating ~~composition~~ by weight or volume.

Claim 68 (currently amended): The coating of claim 1, wherein the active biomolecule comprises 0.001% to 40% of the coating ~~composition~~ by weight or volume.

Claim 69 (original): The coating of claim 1, wherein the biomolecule composition comprises a microorganism based particulate material.

Claim 70 (currently amended): The coating of claim 69, wherein the microorganism based particulate material is a whole cell material.

Claim 71 (currently amended): The coating of ~~claim 70~~ claim 69, wherein the microorganism based particulate material is a cell fragment microorganism based particulate material.

Claim 72 (original): The coating of claim 1, wherein the coating comprises a buffer.

Claim 73 (currently amended): The coating of ~~claim 21~~ claim 72, wherein the buffer comprises a bicarbonate.

Claim 74 (currently amended): The coating of claim 1, wherein the coating is 5 um to 1500 um thick upon ~~the~~ a surface.

Claim 75 (currently amended): The coating of claim 1, wherein the coating is 15 um to 500 um thick upon ~~the~~ a surface.

Claim 76 (original): The coating of claim 1, wherein the coating comprises a paint.

Claim 77 (original): The coating of claim 1, wherein the coating comprises a clear coating.

Claim 78 (original): The coating of claim 77, wherein the clear coating comprises a lacquer, a varnish, a shellac, a stain, a water repellent coating, or a combination thereof.

Claim 79 (original): The coating of claim 1, wherein the coating comprises a multicoat system.

Claim 80 (original): The coating of claim 79, wherein the multicoat system comprises 2 to 10 layers.

Claim 81 (currently amended): The coating of claim 80, wherein one layer of the multicoat system comprises the ~~biomolecular~~ biomolecule composition.

Claim 82 (currently amended): The coating of claim 80, wherein a plurality of layers of the multicoat system comprise the ~~biomolecular~~ biomolecule composition.

Claim 83 (original): The coating of claim 80, wherein each layer of the multicoat system is coating is 15 um to 150 um thick.

Claim 84 (original): The coating of claim 79, wherein the multicoat system comprises a sealer, a water repellent, a primer, an undercoat, or a topcoat.

Claim 85 (original): The coating of claim 79, wherein the multicoat system comprises a topcoat.

Claim 86 (currently amended): The coating of claim 85, wherein the topcoat comprises the ~~biomolecular~~ biomolecule composition.

Claim 87 (original): The coating of claim 1, wherein the coating comprises a binder, a liquid component, a colorant, an additive, or a combination thereof.

Claim 88 (currently amended): The coating of claim 1, wherein the coating is a coating that is capable of ~~undergoes~~ film formation.

Claim 89 (original): The coating of claim 88, wherein film formation occurs at ambient conditions.

Claim 90 (original): The coating of claim 88, wherein film formation occurs at baking conditions.

Claim 91 (original): The coating of claim 90, wherein baking conditions is between 40°C and 50°C.

Claim 92 (original): The coating of claim 90, wherein baking conditions is between 40°C and 65°C.

Claim 93 (original): The coating of claim 90, wherein baking conditions is between 40°C and 110°C.

Claim 94 (original): The coating of claim 88, wherein the coating comprises a volatile component and a non-volatile component.

Claim 95 (original): The coating of claim 94, wherein the coating undergoes film formation by loss of part of the volatile component.

Claim 96 (original): The coating of claim 94, wherein the volatile component comprises a volatile liquid component.

Claim 97 (original): The coating of claim 96, wherein the volatile liquid component comprises a solvent, a thinner, a diluent, or a combination thereof.

Claim 98 (original): The coating of claim 94, wherein the non-volatile component comprises a binder, a colorant, a plasticizer, a coating additive, or a combination thereof.

Claim 99 (original): The coating of claim 88, wherein film formation occurs by crosslinking of a binder.

Claim 100 (original): The coating of claim 99, wherein film formation occurs by crosslinking of a plurality of binders.

Claim 101 (original): The coating of claim 88, wherein film formation occurs by irradiating the coating.

Claim 102 (currently amended): The coating of ~~claim 1~~ claim 88, wherein the coating produces a self-cleaning film.

Claim 103 (original): The coating of claim 1, wherein the coating is a non-film forming coating.

Claim 104 (original): The coating of claim 103, wherein the non-film forming coating comprises a non-film formation binder.

Claim 105 (original): The coating of claim 103, wherein the non-film forming coating comprises a coating component in a concentration that is insufficient to produce a solid film.

Claim 106 (original): The coating of claim 105, wherein the coating component comprises a binder that contributes to thermoplastic film formation.

Claim 107 (original): The coating of claim 105 wherein the coating component contributes to thermosetting film formation.

Claim 108 (original): The coating of claim 107, wherein the coating component comprises a binder, catalyst, initiator, or combination thereof.

Claim 109 (original): The coating of claim 105, wherein the coating component has a concentration of 0%.

Claim 110 (currently amended): The coating of ~~claim 110~~ claim 88, wherein the coating produces a temporary film.

Claim 111 (original): The coating of claim 110, wherein the temporary film has a poor resistance to a coating remover.

Claim 112 (original): The coating of claim 110, wherein the temporary film has a poor scrub resistance, a poor solvent resistance, a poor water resistance, a poor weathering property, a poor adhesion property, or a combination thereof.

Claim 113 (original): The coating of claim 1, wherein the coating comprises an architectural coating, an industrial coating, a specification coating, or a combination thereof.

Claim 114 (currently amended): The coating of ~~claim 1~~ claim 113, wherein the coating comprises an architectural coating.

Claim 115 (original): The coating of claim 114, wherein the architectural coating comprises a wood coating, a masonry coating, an artist's coating, or a combination thereof.

Claim 116 (original): The coating of claim 114, wherein the architectural coating has a pot life of at least 12 months at ambient conditions.

Claim 117 (original): The coating of claim 114, wherein the architectural coating undergoes film formation at ambient conditions.

Claim 118 (currently amended): The coating of ~~claim 1~~ claim 113, wherein the coating comprises an industrial coating.

Claim 119 (original): The coating of claim 118, wherein the industrial coating comprises an automotive coating, a can coating, sealant coating, a marine coating, or a combination thereof.

Claim 120 (currently amended): The coating of ~~claim 119~~ claim 118, wherein the industrial coating undergoes film formation at baking conditions.

Claim 121 (currently amended): The coating of ~~claim 1~~ claim 113, wherein the coating comprises a specification coating.

Claim 122 (currently amended): The coating of claim 121, wherein the specification coating comprises a camouflage coating, a pipeline coating, a traffic marker coating, an aircraft coating, a nuclear power plant coating, or a combination thereof.

Claim 123 (original): The coating of claim 1, wherein the coating comprises a water-borne coating.

Claim 124 (original): The coating of claim 123, wherein the water-borne coating is a latex coating.

Claim 125 (original): The coating of claim 123, wherein the water-borne coating has a density of 1.20 kg/L to 1.50 kg/L.

Claim 126 (original): The coating of claim 1, wherein the coating comprises a solvent-borne coating.

Claim 127 (original): The coating of claim 126, wherein the solvent-borne coating has a density of 0.90 kg/L to 1.2 kg/L.

Claim 128 (original): The coating of claim 1, wherein the coating has a viscosity during application of 72 Ku to 95 Ku.

Claim 129. (original): The coating of claim 1, wherein the coating has a viscosity prior to application of 100 P to 1000 P.

Claim 130 (original): The coating of claim 1, wherein the coating has a viscosity during application of 0.5 P to 2.5 P.

Claim 131. (original): The coating of claim 1, wherein the coating has a viscosity of 100 P to 1000 P upon a surface immediately after application.

Claim 132 (currently amended): The coating of ~~claim 1~~ claim 87, wherein the coating comprises a binder.

Claim 133 (original): The coating of claim 132, wherein the binder comprises a thermoplastic binder, a thermosetting binder, or a combination thereof.

Claim 134 (original): The coating of claim 133, wherein the coating comprises a thermoplastic binder.

Claim 135 (currently amended): The coating of claim 134, wherein the coating is a coating capable of producing ~~produces~~ a film by thermoplastic film formation.

Claim 136 (original): The coating of claim 133, wherein the coating comprises a thermosetting binder.

Claim 137 (currently amended): The coating of claim 136, wherein the coating is a coating capable of producing ~~produces~~ a film by thermosetting film formation.

Claim 138 (original): The coating of claim 132, wherein the binder comprises an oil-based binder.

Claim 139 (original): The coating of claim 138, wherein the oil-based binder comprises an oil, an alkyd, an oleoresinous binder, a fatty acid epoxide ester, or a combination thereof.

Claim 140 (currently amended): The coating of ~~claim 139~~ claim 138, wherein the coating produces a layer 15 um to 25 μm thick upon the vertical surface or 15 um to 40 μm thick upon the horizontal surface.

Claim 141 (original): The coating of claim 132, wherein the binder comprises an oil.

Claim 142 (original): The coating of claim 132, wherein the binder comprises an alkyd.

Claim 143 (original): The coating of claim 132, wherein the binder comprises an oleoresinous binder.

Claim 144 (original): The coating of claim 132, wherein the binder comprises a fatty acid epoxide ester.

Claim 145 (original): The coating of claim 132, wherein the binder comprises a polyester resin.

Claim 146 (original): The coating of claim 145, wherein the polyester resin comprises a hydroxy-terminated polyester.

Claim 147 (original): The coating of claim 145, wherein the polyester resin comprises a carboxylic acid-terminated polyester.

Claim 148 (original): The coating of claim 145, wherein the coating comprises a urethane, an amino resin, or a combination thereof.

Claim 149 (original): The coating of claim 132, wherein the binder comprises a modified cellulose.

Claim 150 (original): The coating of claim 149, wherein the modified cellulose comprises a cellulose ester.

Claim 151 (original): The coating of claim 149, wherein the modified cellulose comprises a nitrocellulose.

Claim 152 (currently amended): The coating of claim 149, wherein the coating comprises an amino binder, an acrylic binder, a urethane binder, or a combination thereof.

Claim 153 (original): The coating of claim 132, wherein the binder comprises a polyamide.

Claim 154 (original): The coating of claim 153, wherein the coating comprises an epoxide.

Claim 155 (original): The coating of claim 132, wherein the binder comprises an amino resin.

Claim 156 (original): The coating of claim 155, wherein the coating comprises an acrylic binder, an alkyd resin, a polyester binder, or a combination thereof.

Claim 157 (currently amended): The coating of claim 132, wherein the binder comprises ~~an~~ a urethane binder.

Claim 158 (original): The coating of claim 157, wherein the coating comprises a polyol, an amine, an epoxide, a silicone, a vinyl, a phenolic, a triacrylate, or a combination thereof.

Claim 159 (original): The coating of claim 132, wherein the binder comprises a phenolic resin.

Claim 160 (original): The coating of claim 159, wherein the coating comprises an alkyd resin, an amino resin, a blown oil, an epoxy resin, a polyamide, a polyvinyl resin, or a combination thereof.

Claim 161 (original): The coating of claim 132, wherein the binder comprises an epoxy resin.

Claim 162 (currently amended): The coating of claim 161, wherein the coating comprises an amino ~~resin~~ resin, a phenolic resin, a polyamide, a ketimine, an aliphatic amine, or a combination thereof.

Claim 163 (original): The coating of claim 161, wherein the epoxy resin comprises a cycloaliphatic epoxy binder.

Claim 164 (original): The coating of claim 163, wherein the coating comprises a polyol.

Claim 165 (original): The coating of claim 132, wherein the binder comprises a polyhydroxyether binder.

Claim 166 (original): The coating of claim 165, wherein the coating comprises an epoxide, a polyurethane comprising an isocyanate moiety, an amino resin, or a combination thereof.

Claim 167 (original): The coating of claim 132, wherein the binder comprises an acrylic resin.

Claim 168 (original): The coating of claim 167, wherein the coating comprises an epoxide, a polyurethane comprising an isocyanate moiety, an amino resin, or a combination thereof.

Claim 169 (original): The coating of claim 132, wherein the binder comprises a polyvinyl binder

Claim 170 (currently amended): The coating of claim 169, wherein the coating comprises an alkyd, ~~an~~ a urethane, an amino-resin, or a combination thereof.

Claim 171 (original): The coating of claim 132, wherein the binder comprises a rubber resin.

Claim 172 (original): The coating of claim 171, wherein the rubber resin comprises a chlorinated rubber resin, a synthetic rubber resin, or a combination thereof.

Claim 173 (original): The coating of claim 171, wherein the coating comprises an acrylic resin, an alkyd resin, a bituminous resin, or a combination thereof.

Claim 174 (original): The coating of claim 132, wherein the binder comprises a bituminous binder.

Claim 175 (original): The coating of claim 174, wherein the coating comprises an epoxy resin.

Claim 176 (original): The coating of claim 132, wherein the binder comprises a polysulfide binder.

Claim 177 (original): The coating of claim 176, wherein the coating comprises a peroxide, a binder comprising an isocyanate moiety, or a combination thereof.

Claim 178 (original): The coating of claim 132, wherein the binder comprises a silicone binder.

Claim 179 (original): The coating of claim 178, wherein the coating comprises an organic binder.

Claim 180 (currently amended): The coating of ~~claim 1~~ claim 87, wherein the coating comprises a liquid component.

Claim 181 (original): The coating of claim 180, wherein the liquid component comprises a solvent, a thinner, a diluent, a plasticizer, or a combination thereof.

Claim 182 (original): The coating of claim 180, wherein the liquid component comprises a liquid organic compound, an inorganic compound, water, or a combination thereof.

Claim 183 (currently amended): The coating of ~~claim 180~~ claim 182, wherein the liquid component comprises a liquid organic compound.

Claim 184 (original): The coating of claim 183, wherein the liquid organic compound comprises a hydrocarbon, an oxygenated compound, a chlorinated hydrocarbon, a nitrated hydrocarbon, a miscellaneous organic liquid component, a plasticizer, or a combination thereof.

Claim 185 (original): The coating of claim 184, wherein the liquid organic compound comprises a hydrocarbon.

Claim 186 (original): The coating of claim 185, wherein the hydrocarbon comprises an aliphatic hydrocarbon, a cycloaliphatic hydrocarbon, a terpene, an aromatic hydrocarbon, or a combination thereof.

Claim 187 (original): The coating of claim 186, wherein the hydrocarbon comprises an aliphatic hydrocarbon.

Claim 188 (currently amended): The coating of claim 187, wherein the aliphatic hydrocarbon comprises a petroleum ether, pentane, hexane, heptane, isododecane, a kerosene, a mineral spirit, a VMP ~~naphthas~~ naphtha, or a combination thereof.

Claim 189 (original): The coating of claim 186, wherein the hydrocarbon comprises a cycloaliphatic hydrocarbon.

Claim 190 (original): The coating of claim 189, wherein the cycloaliphatic hydrocarbon comprises cyclohexane, methylcyclohexane, ethylcyclohexane, tetrahydronaphthalene, decahydronaphthalene, or a combination thereof.

Claim 191 (original): The coating of claim 186, wherein the hydrocarbon comprises a terpene.

Claim 192 (original): The coating of claim 191, wherein the terpene comprises wood terpentine oil, pine oil, α-pinene, β-pinene, dipentene, D-limonene, or a combination thereof.

Claim 193 (original): The coating of claim 186, wherein the hydrocarbon comprises an aromatic hydrocarbon.

Claim 194 (currently amended): The coating of claim 193, wherein the aromatic hydrocarbon comprises benzene, toluene, ethylbenzene, xylene, cumene, a type I high flash aromatic ~~naphthas~~ naphtha, a type II high flash aromatic ~~naphthas~~ naphtha, mesitylene, pseudocumene, cymol, styrene, or a combination thereof.

Claim 195 (currently amended): The coating of claim 184, wherein the liquid organic compound comprises an ~~oxigenated~~ oxygenated compound.

Claim 196 (currently amended): The coating of claim 195, wherein the ~~oxigenated~~ oxygenated compound comprises an alcohol, an ester, a glycol ether, a ketone, an ether, or a combination thereof.

Claim 197 (currently amended): The coating of claim 196, wherein the ~~oxigenated~~ oxygenated compound comprises an alcohol.

Claim 198 (original): The coating of claim 197, wherein the alcohol comprises methanol, ethanol, propanol, isopropanol, 1-butanol, isobutanol, 2-butanol, *tert*-butanol, amyl alcohol, isoamyl alcohol, hexanol, methylisobutylcarbinol, 2-ethylbutanol, isooctyl alcohol, 2-ethylhexanol, isodecanol, cylcohexanol, methylcyclohexanol, trimethylcyclohexanol, benzyl alcohol, methylbenzyl alcohol, furfuryl alcohol, tetrahydrofurfuryl alcohol, diacetone alcohol, trimethylcyclohexanol, or a combination thereof.

Claim 199 (currently amended): The coating of claim 196, wherein the ~~exigenated~~ oxygenated compound comprises an ester.

Claim 200 (original): The coating of claim 199, wherein the ester comprises methyl formate, ethyl formate, butyl formate, isobutyl formate, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, isobutyl acetate, *sec*-butyl acetate, amyl acetate, isoamyl acetate, hexyl acetate, cyclohexyl acetate, benzyl acetate, methyl glycol acetate, ethyl glycol acetate, butyl glycol acetate, ethyl diglycol acetate, butyl diglycol acetate, 1-methoxypropyl acetate, ethoxypropyl acetate, 3-methoxybutyl acetate, ethyl 3-ethoxypropionate, isobutyl isobutyrate, ethyl lactate, butyl lactate, butyl glycolate, dimethyl adipate, glutarate, succinate, ethylene carbonate, propylene carbonate, butyrolactone, or a combination thereof.

Claim 201 (currently amended): The coating of claim 196, wherein the ~~exigenated~~ oxygenated compound comprises a glycol ether.

Claim 202 (original): The coating of claim 201, wherein the glycol ether comprises methyl glycol, ethyl glycol, propyl glycol, isopropyl glycol, butyl glycol, methyl diglycol, ethyl diglycol, butyl diglycol, ethyl triglycol, butyl triglycol, diethylene glycol dimethyl ether, methoxypropanol, isobutoxypropanol, isobutyl glycol, propylene glycol monoethyl ether, 1-isopropoxy-2-propanol, propylene glycol mono-n-propyl ether, propylene glycol n-butyl ether, methyl dipropylene glycol, methoxybutanol, or a combination thereof.

Claim 203 (currently amended): The coating of claim 196, wherein the ~~exigenated~~ oxygenated compound comprises a ketone.

Claim 204 (original): The coating of claim 203, wherein the ketone comprises acetone, methyl ethyl ketone, methyl propyl ketone, methyl isopropyl ketone, methyl butyl ketone, methyl isobutyl ketone, methyl amyl ketone, methyl isoamyl ketone, diethyl ketone, ethyl amyl ketone, dipropyl ketone, diisopropyl ketone, cyclohexanone, methylcylcohexanone, trimethylcyclohexanone, mesityl oxide, diisobutyl ketone, isophorone, or a combination thereof.

Claim 205 (currently amended): The coating of claim 196, wherein the ~~exigenated~~ oxygenated compound comprises an ether.

Claim 206 (original): The coating of claim 205, wherein the ether comprises diethyl ether, diisopropyl ether, dibutyl ether, di-sec-butyl ether, methyl tert-butyl ether, tetrahydrofuran, 1,4-dioxane, metadioxane, or a combination thereof.

Claim 207 (original): The coating of claim 184, wherein the liquid organic compound comprises a chlorinated hydrocarbon.

Claim 208 (original): The coating of claim 207, wherein the chlorinated hydrocarbon comprises methylene chloride, trichloromethane, tetrachloromethane, ethyl chloride, isopropyl chloride, 1,2-dichloroethane, 1,1,1-trichloroethane, trichloroethylene, 1,1,2,2-tetrachlorethane, 1,2-dichloroethylene, perchloroethylene, 1,2-dichloropropane, chlorobenzene, or a combination thereof.

Claim 209 (original): The coating of claim 184, wherein the liquid organic compound comprises a nitrated hydrocarbon.

Claim 210 (original): The coating of claim 209, wherein the nitrated hydrocarbon comprises a nitroparaffin, N-methyl-2-pyrrolidone, or a combination thereof.

Claim 211 (original): The coating of claim 184, wherein the liquid organic compound comprises a miscellaneous organic liquid.

Claim 212 (currently amended): The coating of ~~claim 209~~ claim 211, wherein the miscellaneous organic liquid comprises carbon dioxide; acetic acid, methylal, dimethylacetal, *N*,*N*-dimethylformamide, *N*,*N*-dimethylacetamide, dimethylsulfoxide, tetramethylene suflone, carbon disulfide, 2-nitropropane, *N*-methylpyrrolidone, hexamethylphosphoric triamide, 1,3-dimethyl-2-imidazolidinone, or a combination thereof.

Claim 213 (original): The coating of claim 184, wherein the liquid organic compound comprises a plasticizer.

Claim 214 (original): The coating of claim 213, wherein the plasticizer comprises an adipate, an azelate, a citrate, a chlorinated plasticizer, an epoxide, a phosphate, a sebacate, a phthalate, a polyester, a trimellitate, or a combination thereof.

Claim 215 (currently amended): The coating of ~~claim 180~~ claim 182, wherein the liquid component comprises an inorganic compound.

Claim 216 (original): The coating of claim 215, wherein the inorganic compound comprises ammonia, hydrogen cyanide, hydrogen fluoride, hydrogen cyanide, sulfur dioxide, or a combination thereof.

Claim 217 (currently amended): The coating of ~~claim 180~~ claim 182, wherein the liquid component comprises water.

Claim 218 (original): The coating of claim 217, wherein the liquid component further comprises methanol, ethanol, propanol, isopropyl alcohol, *tert*-butanol, ethylene glycol, methyl glycol, ethyl glycol, propyl glycol, butyl glycol, ethyl diglycol, methoxypropanol, methyldipropylene glycol, dioxane, tetrahydorfuran, acetone, diacetone alcohol, dimethylformamide, dimethyl sulfoxide, ethylbenzene, tetrachloroethylene, *p*-xylene, toluene, diisobutyl ketone, tricholorethylene, trimethylcyclohexanol, cyclohexyl acetate, dibutyl ether, trimethylcyclohexanone, 1,1,1-tricholoroethane, hexane, hexanol, isobutyl acetate, butyl acetate, isophorone, nitropropane, butyl glycol acetate, 2-nitropropane, methylene chloride, methyl isobutyl ketone, cyclohexanone, isopropyl acetate, methylbenzyl alcohol, cyclohexanol, nitroethane, methyl *tert*-butyl ether, ethyl acetate, diethyl ether, butanol, butyl glycolate, isobutanol, 2-butanol, propylene carbonate, ethyl glycol acetate, methyl acetate, methyl ethyl ketone, or a combination thereof.

Claim 219 (original): The coating of claim 87, wherein the coating comprises a colorant.

Claim 220 (currently amended): The coating of claim 219, wherein the colorant comprises a pigment, a dye, or a combination thereof.

Claim 221 (original): The coating of claim 220, wherein the colorant comprises a pigment.

Claim 222 (original): The coating of claim 221, wherein the biomolecule composition comprises 0.001% to 100% of the pigment.

Claim 223 (currently amended): The coating of ~~claim 222~~ claim 221, wherein the pigment volume concentration of the coating is 20% to 60%.

Claim 224 (original): The coating of claim 221, wherein the pigment comprises a corrosion resistance pigment, a camouflage pigment, a color property pigment, an extender pigment, or a combination thereof.

Claim 225 (original): The coating of claim 224, wherein the pigment comprises a corrosion resistance pigment.

Claim 226 (original): The coating of claim 225, wherein the corrosion resistance pigment comprises aluminum flake, aluminum triphosphate, aluminum zinc phosphate, ammonium chromate, barium borosilicate, barium chromate, barium metaborate, basic calcium zinc molybdate, basic carbonate white lead, basic lead silicate, basic lead silicochromate, basic lead silicosulfate, basic zinc molybdate, basic zinc molybdate-phosphate, basic zinc molybdenum phosphate, basic zinc phosphate hydrate, bronze flake, calcium barium phosphosilicate, calcium borosilicate, calcium chromate, calcium plumbate, calcium strontium phosphosilicate, calcium strontium zinc phosphosilicate, dibasic lead phosphite, lead chromosilicate, lead cyanamide, lead suboxide, lead sulfate, mica, micaceous iron oxide, red lead, steel flake, strontium borosilicate, strontium chromate, tribasic lead phophosilicate, zinc borate, zinc borosilicate, zinc chromate, zinc dust, zinc hydroxy phosphite, zinc molybdate, zinc oxide, zinc phosphate, zinc potassium chromate, zinc silicophosphate hydrate, zinc tetraoxylchromate, or a combination thereof.

Claim 227 (original): The coating of claim 225, wherein the coating is a metal surface coating.

Claim 228 (original): The coating of claim 225, wherein the coating is a primer.

Claim 229 (original): The coating of claim 224, wherein the pigment comprises a camouflage pigment.

Claim 230 (original): The coating of claim 229, wherein the camouflage pigment comprises an anthraquinone black, a chromium oxide green, or a combination thereof.

Claim 231 (original): The coating of claim 224, wherein the pigment comprises a color property pigment.

Claim 232 (original): The coating of claim 231, wherein the color property pigment comprises a black pigment, a brown pigment, a white pigment, a pearlescent pigment, a violet pigment, a blue pigment, a green pigment, a yellow pigment, an orange pigment, a red pigment, a metallic pigment, or a combination thereof.

Claim 233 (currently amended): The coating of claim 232, wherein the color property pigment comprises aniline black; anthraquinone black; carbon black; copper carbonate; graphite; iron oxide; micaceous iron oxide; manganese dioxide, azo condensation~~,benzimidazolone, iron oxide~~; metal complex brown; antimony oxide; basic lead carbonate; lithopone; titanium dioxide; white lead; zinc oxide; zinc sulphide; titanium dioxide and ferric oxide covered mica, bismuth oxychloride crystal, ~~dioxanine~~ dioxazine violet~~, carbazol Blue~~; carbazole Blue; cobalt blue; ~~copper phthalocyanine; dioxanine Blue;~~ indanthrone; ~~phthalocyanin~~ phthalocyanine blue; Prussian blue; ultramarine; chrome green; ~~chromium oxide green; halogenated copper phthalocyanine;~~ hydrated chromium oxide; phthalocyanine green; anthrapyrimidine; arylamide yellow; barium chromate; benzimidazolone yellow; bismuth vanadate; cadmium sulfide yellow; complex inorganic color ~~pigment~~; diarylide yellow; disazo condensation; flavanthrone; isoindoline; isoindolinone; lead chromate; nickel azo yellow; organic metal complex; ~~quinophthalone;~~ yellow iron oxide; ~~yellow oxide;~~ zinc chromate; perinone orange; pyrazolone orange; anthraquinone; benzimidazolone; BON arylamide; cadmium red; cadmium selenide; chrome red; dibromanthrone; diketopyrrolo-pyrrole ~~pigment; disazo condensation pigment~~; lead molybdate; perylene; pyranthrone; quinacridone; quinophthalone; red iron oxide; red lead; toluidine red; tonor ~~pigment~~; β-naphthol red; aluminum flake; aluminum non-leafing, gold bronze flake, zinc dust, stainless steel flake, nickel flake, nickel powder, or a combination thereof.

Claim 234 (original): The coating of claim 224, wherein the pigment comprises an extender pigment.

Claim 235 (currently amended): The coating of claim 234, wherein the extender pigment comprises a barium sulphate, a calcium carbonate, a kaolin, a calcium-~~sulphat~~ sulphate, a silicate, a silica, an alumina trihydrate; or a combination thereof.

Claim 236 (original): The coating of claim 87, wherein the coating comprises an additive.

Claim 237 (original): The coating of claim 236, wherein the additive comprises 0.001% to 20.0% by weight, of the coating.

Claim 238 (original): The coating of claim 236, wherein said additive comprises an accelerator, an adhesion promoter, an antifoamer, anti-insect additive, an antioxidant, an antiskinning agent, a buffer, a catalyst, a coalescing agent, a corrosion inhibitor, a defoamer, a dehydrator, a dispersant, a drier, electrical additive, an emulsifier, a filler, a flame/fire retardant, a flatting agent, a flow control agent, a gloss aid, a leveling agent, a marproofing agent, a preservative, a silicone additive, a slip agent, a surfactant, a light stabilizer, a rheological control agent, a wetting additive, or a combination thereof.

Claim 239 (currently amended): The coating of ~~claim 236~~ claim 238, wherein the additive comprises a preservative.

Claim 240 (original): The coating of claim 239, wherein the preservative comprises an in-can preservative, an in-film preservative, or a combination thereof.

Claim 241 (original): The coating of claim 239, wherein the preservative comprises a biocide.

Claim 242 (original): The coating of claim 241, wherein the biocide comprises a bactericide, a fungicide, an algaecide, or a combination thereof.

Claim 243 (currently amended): The coating of ~~claim 236~~ claim 238, wherein the additive comprises a wetting additive, a dispersant, or a combination thereof.

Claim 244 (currently amended): The coating of ~~claim 236~~ claim 238, wherein the additive comprises an ~~anti-foamer~~ antifoamer, a defoamer, or a combination thereof.

Claim 245 (original): The coating of claim 238, wherein the additive comprises a rheological control agent.

Claim 246 (original): The coating of claim 245, wherein the rheological control agent comprises a thickener, a viscosifier, or a combination thereof.

Claim 247 (original): The coating of claim 238, wherein the additive comprises a corrosion inhibitor.

Claim 248 (original): The coating of claim 247, wherein said corrosion inhibitor comprises an in-can corrosion inhibitor, a flash corrosion inhibitor, or a combination thereof.

Claim 249 (original): The coating of claim 238, wherein the additive comprises a light stabilizer.

Claim 250 (original): The coating of claim 249, wherein the light stabilizer comprises a UV absorber, a radical scavenger, or a combination thereof.

Claim 251 (original): The coating of claim 1, wherein the coating is a multi-pack coating.

Claim 252 (currently amended): The coating of claim 251, wherein the multi-pack coating is stored in a two to five containers prior to application to ~~the~~ a surface.

Claim 253 (currently amended): The coating of claim 251, wherein 0.001% to 100% of the ~~biomolecular~~ biomolecule composition is stored in a container of ~~a~~ the multi-pack coating, and at least one additional coating component is stored in another container of ~~a~~ the multi-pack coating.

Claim 254 (currently amended): The coating of claim 253, wherein the container ~~comprising~~ that stores the ~~biomolecular~~ biomolecule composition further ~~comprises~~ stores an additional coating component.

Claim 255 (original): The coating of claim 254, wherein the additional coating component comprises a preservative, a wetting agent, a dispersing agent, a buffer, a liquid component, a rheological modifier, or a combination thereof.

Claim 256 (currently amended): The coating of ~~claim 255~~ claim 254, wherein the additional coating component comprises glycerol.

Claim 257 (currently amended): A method of detoxification of a surface contaminated with an organophosphorus compound, comprising the ~~steps~~ step of: contacting a surface contaminated with an organophosphorous compound with a coating comprising a biomolecule composition, wherein the biomolecule composition comprises a phosphoric triester hydrolase.

Claim 258 (original): The method of claim 257, wherein said organophosphorus compound comprises a chemical warfare agent.

Claim 259 (original): The method of claim 258, wherein the chemical warfare agent comprises a persistent agent.

Claim 260 (original): The method of claim 258, wherein the chemical warefare agent comprises a G-agent, a V agent, or a combination thereof.

Claim 261 (original): The method of claim 260, wherein said G-agent comprises soman, sarin, cyclosarin, tabun, or a combination thereof.

Claim 262 (original): The method of claim 260, wherein said V-agent comprises VX, Russian VX, or a combination thereof.

Claim 263 (original): The method of claim 257, wherein said organophosphorus compound comprises a pesticide.

Claim 264 (original): The method of claim 263, wherein the pesticide comprises a persistent organophosphorous compound.

Claim 265 (currently amended): The method of ~~claim 258~~ claim 263, wherein the pesticide comprises bromophos-ethyl, chlorpyrifos, chlorfenvinphos, chlorothiophos, chlorpyrifos-methyl, coumaphos, crotoxyphos, crufomate, cyanophos, diazinon, dichlofenthion, dichlorvos, ~~dursban,~~ EPN, ethoprop~~, ethyl-parathion~~, etrimifos, famphur, fensulfothion, fenthion, fenthrothion, isofenphos, jodfenphos, leptophos-oxon, malathion, methyl-parathion, mevinphos, paraoxon, parathion~~, parathion-methyl~~, pirimiphos-ethyl, pirimiphos-methyl, pyrazophos, quinalphos, ronnel, sulfopros, sulfotepp, trichloronate, or a combination thereof.

Claim 266 (original): The method of claim 257, wherein the method further comprises the step of contacting the surface with a caustic agent; a decontaminating foam, a combination of baking condition heat and carbon dioxide, or a combination thereof.

Claim 267 (currently amended): A method of detoxification of an organophosphorus compound, comprising the ~~steps~~ step of: contacting an organophosphorous compound with a coating comprising a biomolecule composition, wherein the biomolecule composition comprises a phosphoric triester hydrolase.

Claim 268 (original): A method of reducing the concentration of an organophosphorus compound upon a surface, comprising the steps of: applying to the surface a coating comprising a biomolecule composition, wherein the biomolecule composition comprises a phosphoric triester hydrolase, and contacting the surface with an organophosphorus compound.

Claim 269 (original): A coating comprising 0.001% to 40% by weight or volume a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 270 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises a proteinaceous molecule that binds a ligand.

Claim 271 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises an enzyme.

Claim 272 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises a phosphoric triester hydrolase.

Claim 273 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises an organophosphorus hydrolase.

Claim 274 (original): A coating comprising a biomolecule composition, wherein the biomolecule composition comprises an organophosphorus hydrolase and a buffer.

Claim 275 (original): A coating comprising a microorganism based particulate material, wherein the microorganism based particulate material that comprises an active biomolecule.

Claim 276 (original): A coating comprising a whole cell particulate material, wherein the particulate material comprises an active biomolecule.

Claim 277 (original): A coating comprising 0.001% to 40% by weight or volume of a whole cell particulate material, wherein the whole cell particulate material comprises an active biomolecule.

Claim 278 (original): A coating comprising a whole cell particulate material, wherein the particulate material comprises an enzyme.

Claim 279 (original): A coating comprising a whole cell particulate material, wherein the particulate material comprises a phosphoric triester hydrolase.

Claim 280 (original): A coating comprising a whole cell particulate material, wherein the particulate material comprises an organophosphorus hydrolase.

Claim 281 (original): A coating comprising a whole cell particulate material, wherein the particulate material comprises an organophosphorus hydrolase and a buffer.

Claim 282 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 283 (original): A coating, the improvement comprising inclusion of 0.001% to 40% by weight or volume a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 284 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises a proteinaceous molecule that binds a ligand.

Claim 285 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises an enzyme.

Claim 286 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises a phosphoric triester hydrolase.

Claim 287 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises an organophosphorus hydrolase.

Claim 288 (original): A coating, the improvement comprising inclusion of a biomolecule composition, wherein the biomolecule composition comprises an organophosphorus hydrolase and a buffer.

Claim 289 (original): A coating, the improvement comprising inclusion of a microorganism based particulate material, wherein the microorganism based particulate material that comprises an active biomolecule.

Claim 290 (original): A coating, the improvement comprising inclusion of a whole cell particulate material, wherein the particulate material comprises an active biomolecule.

Claim 291 (original): A coating, the improvement comprising inclusion of 0.001% to 40% by weight or volume of a whole cell particulate material, wherein the whole cell particulate material comprises an active biomolecule.

Claim 292 (original): A coating, the improvement comprising inclusion of a whole cell particulate material, wherein the particulate material comprises an enzyme.

Claim 293 (original): A coating, the improvement comprising inclusion of a whole cell particulate material, wherein the particulate material comprises a phosphoric triester hydrolase.

Claim 294 (original): A coating, the improvement comprising inclusion of a whole cell particulate material, wherein the particulate material comprises an organophosphorus hydrolase.

Claim 295 (original): A coating, the improvement comprising inclusion of a whole cell particulate material, wherein the particulate material comprises an organophosphorus hydrolase and a buffer.

Claim 296 (original): A water-borne paint comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 297 (original): A solvent-borne paint comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 298 (original): A latex paint comprising a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 299 (original): An oil-based paint comprising a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 300 (original): A latex paint comprising a whole cell particulate material and a buffer, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 301 (original): An oil-based paint comprising a whole cell particulate material and a buffer, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 302 (original): An latex paint comprising 0.001% to 40% by weight or volume of a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 303 (original): An oil-based paint comprising 0.001% to 40% by weight or volume of a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 304 (original): A multi-pack latex paint, wherein one container comprises 0.001% to 40%, by weight or volume of the paint, a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 305 (original): A multi-pack oil-based paint, wherein one container comprises 0.001% to 40%, by weight or volume of the paint, a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase.

Claim 306 (original): A multi-pack latex paint, wherein one container comprises 0.001% to 40%, by weight or volume of the paint, a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase, and wherein the container comprising the whole cell particulate material further comprises a preservative, a wetting agent, a dispersing agent, a buffer, a liquid component, a rheological modifier, or a combination thereof.

Claim 307 (original): A multi-pack oil-based paint, wherein one container comprises 0.001% to 40%, by weight or volume of the paint, a whole cell particulate material, wherein the whole cell particulate material comprises a phosphoric triester hydrolase, and wherein the container comprising the whole cell particulate material further comprises a preservative, a wetting agent, a dispersing agent, a buffer, a liquid component, a rheological modifier, or a combination thereof.

Claim 308 (currently amended): A two-pack latex paint, wherein one container comprises 100 parts by volume paint, wherein a second container comprises three parts by volume of a ~~biomolecular~~ biomolecule composition comprising a whole cell particulate material, wherein the whole cell particulate material comprises an organophosphorus hydrolase, and wherein each part of the ~~biomolecular~~ biomolecule composition comprises 1 mg per milliliter of whole cell particulate material and 50% glycerol.

Claim 309 (currently amended): An two-pack oil-based paint, wherein one container comprises 100 parts by volume paint, wherein a second container comprises three parts by volume of a ~~biomolecular~~ biomolecule composition comprising a whole cell particulate material, wherein the whole cell particulate material comprises an organophosphorus hydrolase, and wherein each part of the ~~biomolecular~~ biomolecule composition comprises 1 mg per milliliter of whole cell particulate material and 50% glycerol.

Claim 310 (currently amended): A two-pack latex paint, wherein one container comprises 100 parts by volume paint, wherein a second container comprises three parts by volume of a ~~biomolecular~~ biomolecule composition comprising a whole cell particulate material, wherein the whole cell particulate material comprises an organophosphorus hydrolase, wherein each part of the ~~biomolecular~~ biomolecule composition comprises 1 mg per milliliter of whole cell particulate material, wherein the paint comprises a buffer, and wherein the buffer comprises ammonium bicarbonate, a monobasic buffer, a dibasic phosphate buffer, Trizma base, a five zwitterionic buffer, or a combination thereof.

Claim 311 (currently amended): An two-pack oil-based paint, wherein one container comprises 100 parts by volume paint, wherein a second container comprises three parts by volume of a ~~biomolecular~~ biomolecule composition comprising a whole cell particulate material, wherein the whole cell particulate material comprises an organophosphorus hydrolase, wherein each part of the ~~biomolecular~~ biomolecule composition comprises 1 mg per ~~milliliterof~~ milliliter of whole cell particulate material, wherein the paint comprises a buffer, and wherein the buffer comprises ammonium bicarbonate, a monobasic buffer, a dibasic phosphate buffer, Trizma base, a five zwitterionic buffer, or a combination thereof.

Claim 312 (original): A non-film forming coating comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 313 (original): An elastomer comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 314 (original): A filler comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 315 (original): An adhesive comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 316 (original): A sealant comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 317 (original): A material applied to a textile, comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 318 (original): A wax comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 319 (original): A surface treatment comprising a biomolecule composition, wherein the biomolecule composition comprises an active biomolecule.

Claim 320 (currently amended): A surface treatment of ~~Claim~~ claim 319, wherein the surface treatment is a coating, a paint, a non-film forming coating, an elastomer, an adhesive, an sealant, a material applied to a textile, or a wax.

Claim 321 (currently amended): The surface treatment of ~~Claim~~ claim 320, wherein the surface treatment comprises a pH indicator.

Claim 322 (new): The coating of claim 45, wherein the organophosphorus acid anhydrolase comprises an *Acinetobacter calcoaceticus* ATCC 19606 OPAA, an *Aeromonas hydrophila* ATCC 7966 OPAA, an *Aeromonas proteolytica* OPAA, an *Arm. A* isolate 1 OPAA, an *Arm. A* isolate 2 OPAA, a *Bacillus subtilis* (fr. Zuberer) OPAA, a *Bacillus subtilis* OPAA, a ATCC 18685 OPAA, a *Bacillus subtilis* BRB41 OPAA, a *Bacillus subtilis* Q OPAA, a *Bacillus thuringensis* (fr. Zuberer) OPAA, a *Burkholderia cepacia* LB400 OPAA, a *Burkholderia cepacia* T OPAA, a *Citrobacter diversus* OPAA, a *Citrobacter freundii* ATCC 8090 OPAA, an *Edwardsiella tarda* ATCC 15947 OPAA, an *Enterobacter aerogenes* ATCC 13048 OPAA, an *Enterobacter cloacae* 96-3 OPAA, an *Enterobacter liquefaciens* 363 OPAA, an *Enterobacter liquefaciens* 670 OPAA, an *Erwinia carotovora* EC189-67 OPAA, an *Erwinia herbicola* OPAA, an *Erwinia herbicola* (*agglomerans*) OPAA, an *Escherichia coli* E63 OPAA, a *Hafnia alvei* ATCC 13337 OPAA, a *Klebsiella pneumoniae* ATCC 13883 OPAA, a *Lactobacillus casei* 686 OPAA, a *Lactococcus lactis* subsp. *lactis* pIL253 OPAA, a *Proteus morganaii* OPAA, a *Proteus vulgaris* ATCC 13315 OPAA, a *Pseudomonas aeriginosa* ATCC 10145 OPAA, a *Pseudomonas aeriginosa* ATCC 27853 OPAA, a *Pseudomonas flourescens* OPAA, a *Pseudomonas putida* ATCC 18633 OPAA, a *Pseudomonas putida* PpY101 OPAA, a *Pseudomonas* sp. P OPAA, a *Salmonella typhimurium* ATCC 14028 OPAA, a *Serratia marcescens* ATCC 8100 OPAA, a *Serratia marcescens* HY OPAA, a *Serratia marcescens* Nima OPAA, a *Shigella flexneri* ATCC 12022 OPAA, a *Shigella sonnei* ATCC 25931 OPAA, a *Staphylococcus aureus* ATCC 25923 OPAA, a *Staphylococcus* sp. S OPAA, a *Streptococcus faecalis* ATCC 19433 OPAA, a *Vibrio parahaemolyticus* TAMU 109 OPAA, a *Yersinia enterocolitica* ATCC 9610 OPAA, a *Yersinia enterocolitica* TAMU 84 OPAA, a *Yersinia frederiksenii* TAMU 91 OPAA, a *Yersinia intermedia* ATCC 29909 OPAA, a *Yersinia intermedii* TAMU 86 OPAA, a *Yersinia kristensenia* ATCC 33640 OPAA, a *Yersinia kristensenia* TAMU 95 OPAA, a *Yersinia* sp. ATCC 29912 OPAA, a *Vibrio proteolyticus* ATCC 15338 OPAA, a *Thermus* sp. ATCC 31674 OPAA, a *Streptomyces cinnamonensis* subsp. *Proteolyticus* ATCC 19893 OPAA, a *Deinococcus proteolyticus* ATCC 35074 OPAA, a *Clostridium proteolyticum* ATCC 49002 OPAA, an *Aeromonas jandaei* ATCC 49568 OPAA, an *Aeromonas veronii* biogroup *sobria* ATCC 9071 OPAA, a *Pseudoaltermonas haloplanktis* ATCC 23821 OPAA, a *Xanthomonas campestris* ATCC 33913 OPAA, a *Pseudoalteromonas espejiana* ATCC 27025 OPAA, a *Shewanella putrefasciens* ATCC 8071 OPAA, a *Stenotrophomonas maltophilus* ATCC 13637 OPAA, an *Ochrobactrum anthropi* ATCC 19286 OPAA, a *Desulfovibrio vulgaris* OPAA, or a combination thereof.

Claim 323 (new): The coating of claim 73, wherein the biocarbonate comprises an ammonium bicarbonate.

Claim 324 (new): The coating of claim 72, wherein the buffer comprises a monobasic phosphate buffer, a dibasic phosphate buffer, Trizma base, a 5 zwitterionic buffer, triethanolamine, or a combination thereof.

Claim 325 (new): The coating of claim 213, wherein the plasticizer comprises di(2-ethylhexyl) azelate; di(butyl) sebacate; di(2-ethylhexyl) phthalate; di(isononyl) phthalate; dibutyl phthalate; butyl benzyl phthalate; di(isooctyl) phthalate; di(idodecyl) phthalate; tris(2-ethylhexyl) trimellitate; tris(isononyl) trimellitate; di(2-ethylhexyl) adipate; di(isononyl) adipate; acetyl tri-*n*-butyl citrate; an epoxy modified soybean oil; 2-ethylhexyl epoxytallate; isodecyl diphenyl phosphate; tricresyl phosphate; isodecyl diphenyl phosphate; tri-2-ethylhexyl phosphate; an adipic acid polyester; an azelaic acid polyester; or a bisphenoxyethylformal.

Claim 326 (new): The coating of claim 221, wherein the pigment comprises barium ferrite; borosilicate; burnt sienna; burnt umber; calcium ferrite; cerium; chrome orange; chrome yellow; chromium phosphate; cobalt-containing iron oxide; fast chrome green; gold bronze powder; luminescent; magnetic; molybdate orange; molybdate red; oxazine; oxysulfide; polycyclic; raw sienna; surface modified pigment; thiazine; thioindigo; transparent cobalt blue; transparent cobalt green; transparent iron blue; transparent zinc oxide; triarylcarbonium; zinc cyanamide; or zinc ferrite.

Claim 327 (new): The coating of claim 229, wherein the camouflage pigment reduces the ability of the coating to be detected by a devise that measures infrared radiation.

Claim 328 (new): The coating of claim 239, wherein the preservative comprises 1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride; 1,2-benzisothiazoline-3-one; 1,2-dibromo-2,4-dicyanobutane; 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin; 1-methyl-3,5,7-triaza-1-azonia-adamantane chloride; 2-(4-thiazolyl)benzimidazole; 2-(hydroxymethyl)-amino-2-methyl-1-propanol; 2(hydroxymethyl)-aminoethanol; 2,2-dibromo-3-nitrilopropionamide; 2,4,5,6-tetrachloro-isophthalonitrile; 2-mercaptobenzo-thiazole; 2-methyl-4-isothiazolin-3-one; 2-n-octyl-4-isothiazoline-3-one; 3-iodo-2-propynl N-butyl carbamate; 4,4-dimethyloxazolidine; 5-chloro-2-methyl-4-isothiazolin-3-one; 5-hydroxy-methyl-1-aza-3,7-dioxabicylco (3.3.0.) octane; 6-acetoxy-2,4-dimethyl-1,3-dioxane; 7-ethyl bicyclooxazolidine; a combination of 2-(thiocyanomethyl-thio)benzothiozole and methylene bis(thiocyanate); a combination of 4-(2-nitrobutyl)-morpholine and 4,4'-(2-ethylnitrotrimethylene) dimorpholine; a combination of 4,4-dimethyl-oxazolidine and 3,4,4-trimethyloxazolidine; a combination of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one; a combination of chlorothalonil and 3-iodo-2-propynl N-butyl carbamate; a combination of chlorothalonil and a triazine compound; a combination of tributyltin benzoate and alkylamine hydrochlorides; a combination of zinc-dimethyldithiocarbamate and zinc 2-mercaptobenzothiazole; a copper soap; a metal soap, a mercury soap; a mixture of bicyclic oxazolidines; a tin soap; an alkylamine hydrochloride; an amine reaction product; barium metaborate; butyl parahydroxybenzoate; copper(II) 8-quinolinolate; diiodomethyl-p-tolysulfone; ethyl parahydroxybenzoate; glutaraldehyde; hexahydro-1,3,5-triethyl-s-triazine; hydroxymethyl-5,5-dimethylhydantoin; methyl parahydroxybenzoate; N-(trichloromethylthio) phthalimide; N-cyclopropyl-N-(1-dimethylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine; N-trichloromethyl-thio-4-cyclohexene-1,2-dicarboximide; p-chloro-m-cresol; phenylmercuric acetate; potassium dimethyldithiocarbamate; potassium N-hydroxy-methyl-N-methyl-dithiocarbamate; propyl parahydroxybenzoate; sodium 2-pyridinethiol-1-oxide; tetra-hydro-3,5-di-methyl-2H-1,3,5-thiadiazine-2-thione; tributyltin benzoate; tributyltin oxide; tributyltin salicylate; zinc 2-pyridinethiol-N-oxide; zinc oxide; or a zinc soap.

Claim 329 (new): The coating of claim 243, wherein the additive comprises a combination of an unsaturated polyamine amide salt and a lower molecular weight acid; a polycarboxylic acid polymer alkylolammonium salt; a combination of a long chain polyamine amide salt and a polar acidic ester; a hydroxyfunctional carboxylic acid ester; or a non-ionic wetting agent.

Claim 330 (new): The coating of claim 243, wherein the additive comprises a wetting additive.

Claim 331 (new): The coating of claim 330, wherein the wetting additive comprises an ethylene oxide molecule comprising a hydrophobic moiety; a surfactant; pine oil; a metal soap; calcium octoate; zinc octoate; aluminum stearate; zinc stearate; bis(2-ethylhexyl)sulfosuccinate; (octylphenoxy)polyethoxyethanol octylphenyl-polyethylene glycol; nonyl phenoxy poly (ethylene oxy) ethanol; or ethylene glycol octyl phenyl ether.

Claim 332 (new): The coating of claim 243, wherein the additive comprises a dispersant.

Claim 333 (new): The coating of claim 332, wherein the dispersant comprises tetra-potassium pyrophosphate, a phosphate ester surfactant; a particulate material, a calcium carbonate coated with fatty acid, a modified montmorillonite clay, or a caster wax.

Claim 334 (new): The coating of claim 244, wherein the additive comprises an oil; a mineral oil; a silicon oil; a fatty acid ester; dibutyl phosphate; a metallic soap; a siloxane; a wax; an alcohol comprising six to ten carbons; or a pine oil.

Claim 335 (new): The coating of claim 244, wherein the coating further comprises an emulsifier, a hydrophobic silica, or a combination thereof.

Claim 336 (new): The composition of claim 245, wherein the rheology control agent comprises a silicate; a montmorillonite silicate; aluminum silicate, a bentonite, magnesium silicate, a cellulose ether, a hydrogenated oil, a polyacrylate, a polyvinylpyrrolidone, a urethane, a methyl cellulose, a hydroxyethyl cellulose, hydrogenated castor oil; a hydrophobically modified ethylene oxide urethane; a titanium chelate, or a zirconium chelate.

Claim 337 (new): The coating of claim 247, wherein the corrosion inhibitor comprises a chromate, a phosphate, a molybdate, a wollastonite, a calcium ion-exchanged silica gel, a zinc compound, a borosilicate, a phosphosilicate, a hydrotalcite, or a combination thereof.

Claim 338 (new): The coating of claim 248, wherein the corrosion inhibitor comprises sodium nitrate, sodium benzoate, ammonium benzoate, or 2-amino-2-methyl-propan-1-ol.

Claim 339 (new): The coating of claim 250, wherein the light stabilizer comprises a UV absorber.

Claim 340 (new): The coating of claim 339, wherein the UV absorber comprises a hydroxybenzophenone, a hydroxyphenylbenzotriazole, a hydrozyphenyl-S-triazine, an oxalic anilide, yellow iron oxide, or a combination thereof.

Claim 341 (new): The coating of claim 250, wherein the light stabilizer comprises a radical scavenger.

Claim 342 (new): The coating of claim 341, wherein the radical scavenger comprises a sterically hindered amine; bis(1,2,2,6,6,-pentamethyl-4-poperidinyl) ester, or bis(2,2,6,6,-tetramethyl-1-isooctyloxy-4-piperidinyl) ester.

Claim 343 (new): The coating of claim 1, wherein the coating is a coating capable of being applied to a surface by a spray applicator.

Claim 344 (new): The coating of claim 1, wherein the biomolecule composition is microencapsulated.

Claim 345 (new): The coating of claim 1, wherein the coating comprises a pH indicator.

Claim 346 (new): The coating of claim 345, wherein the pH indicator is a colormetric indicator.

Claim 347 (new): The coating of claim 346, wherein the colormetric indicator comprises Alizarin, Alizarin S, Brilliant Yellow, Lacmoid, Neutral Red, Rosolic Red, or a combination thereof.

Claim 348 (new): The coating of claim 345, wherein the pH indicator is a fluorimetric indicator.

Claim 349 (new): The coating of claim 348, wherein the fluorimetric indicator comprises SNARF-1, BCECF, HPTS, Fluroescein, or a combination thereof.

Claim 350 (new): The coating of claim 345, wherein the pH indicator is a pH indicator that undergoes a color or fluorescence change between pH 8 to pH 9.

REMARKS/ARGUMENTS

Claims 1-350 remain in this application.

Claim 322 has been added to specify an embodiment of the invention of the above-cited application described at page 243, lines 9-40. Claims 323 and 324 have been added to specify embodiments described at page 200, lines 14-19. Claim 325 has been added to specify embodiments described at page 172, line 36 to page 173, line 12. Claim 326 has been added to specify embodiments described at page 175, line 35 to page 176, line 33. Claim 327 has been added to specify an embodiment described at page 107, lines 15-20. Claim 328 has been added to specify embodiments described at page 194, line 23 to page 196, line 45. Claims 329, 330, 331, 332, and 333 have been added to specify embodiments described at page 197, line 46 to page 200, line 2. Claims 334 and 335 have been added to specify embodiments described at page 203, lines 21-30. Claim 336 has been added to specify embodiments described at page 202, lines 11-36. Claims 337 and 338 have been added to specify embodiments described at page 207, line 41 to page 208, line 15. Claims 339, 340, 341, and 342 have been added to specify embodiments described at page 207, lines 6-23. Claim 343 has been added to specify an embodiment described at page 88, lines 23-31. Claim 344 has been added to specify an embodiment described at page 81, lines 4-15. Claims 345 to 350 have been added to specify an embodiments described at page 26, line 14 to page 27, line 9.

Claims 40, 63 and 122 have been revised to specify an embodiment of the invention described at page 17, lines 18-20; at page 48, lines 3-8; and page 21, lines 24-26, respectively. Claims 308, 309, 310, and 311 have been revised to specify embodiments of the present invention described at page 31, lines 1-29, at page 84, lines 3-15, at page 231, lines 18-21, and at originally filed claim 311, and these claims have been revised to conform the claim language to the language of the other claims. Claims 42, 54, 233 and 265 have been revised to remove duplicative words or phrases. Claims 6, 7, 9, 10, 18, 19, 25, 31, 34, 37, 40, 55, 59, 63, 64, 71, 73, 102, 110, 114, 118, 120, 121, 132, 140, 180, 183, 212, 215, 217, 223, 239, 243, 244, 256, and 265 are dependent claims, and have been revised in dependency to more clearly delineate the various embodiments of the invention. Claims 23, 195, 196, 197, 199, 201, 203, 205, 235, 244, 320 and 321 have been revised to correct typographical errors. Claims 70, 88, 122, 135, 137, 152, 157, 162, 170, 188, 194, 220, 257, and 267, have been grammatically revised to more clearly claim an embodiment of the present invention described within each of the respective claims. Claims 67, 68, 74, 75, 81, 82, 86, 252, 253, and 254 have been revised in antecedent basis to more clearly claim an embodiment of the present invention described within each of the respective claims.

These revisions to the claims and added new claims are supported by the above cited patent application, and do not constitute new matter. If any additional fee is required, the Office is requested to debit U.S.P.T.O. Account No. 50-1085 for such fees.

Respectfully Submitted,

MCDANIEL & ASSOCIATES

By_____

C. Steven McDaniel
Attorney for Applicant
Reg. No. 33,962
Tel.: (512) 472-8282

Example 6
NATO Demonstration of Soman Detoxification Using OPH-Painted Surfaces

At the September 22, 2002, meeting of the NATO Army Armaments Group in Cazaux, France, painted metal surfaces were assayed with soman using standard NATO procedures and protocols. For the assays, 10 cm x 10 cm metal plates primed with standard NATO specification paints were coated with paint containing OPH. Control plates plus two different versions of the OPH enzyme composition differing in soman detoxification specificity were used. These surfaces were allowed to dry for several hours at room temperature and then assayed according to standard NATO assay protocol (described below), modified to account for the unique character of the surfaces treated with a paint comprising OPH.

The form of OPH in the biomolecular composition contains both the changes of the previously described H254R mutant and the H257L mutant, and is corresponding designated the "H254R, H257L mutant." The H254R, H257L mutant demonstrates a several-fold enhanced rates of R-VX catalysis relative to either the H254R mutant or the H257L mutant, and a 20-fold enhancement of activity relative to wild-type OPH. This version of the OPH biomolecular composition has been assayed in paints treated with soman or R-VX, and are described below.

Following standard protocols, OPD painted surfaces were uniformly contaminated with an isopropanol solution containing the chemical warfare agent soman. The concentration of soman on each contaminated surface was 1.0 mg/cm^2. The contaminated plates were maintained at or slightly above room temperature (≥20°C) without any forced air-flow for various periods of time. A zero-time, 15 minutes, 30 minutes, and 45 minutes sample was taken for each control and biomolecular composition-containing plate series. In order to terminate the reaction and isolate residual soman on the plate surface, each plate was submerged in a container of isopropanol at the end-point and placed on a shaker to thoroughly extract any residual nerve agent. The solubilized portions were then quantified for soman. These assays showed that both the forms of OPH biomolecular composition were highly effective in detoxifying soman on metal surfaces. The two different OPH biomolecular compositions assayed detoxified the soman at levels over 65% and 77% after 45 minutes (Nato Army Armaments Group Project Group 31 on Non-Corrosive, Biotechnology-Based Decontaminants for CBW Agents, 2002). Additional assays with a CWA simulant indicated that had the NATO assay run for one to two hours, substantially all of the soman would have been detoxified.

Organophosphates

Last Updated: March 14, 2003

Synonyms and related keywords: nerve agent, pesticides

AUTHOR INFORMATION

Author: **Frances M Dyro, MD**, Chief of the Neuromuscular Section, Associate Professor, Department of Neurology, New York Medical College, Westchester Medical Center

Frances M Dyro, MD, is a member of the following medical societies: American Academy of Neurology, American Association of Electrodiagnostic Medicine, and Muscular Dystrophy Association

Editor(s): **Jonathan S Rutchik, MD, MPH**, Assistant Professor, Department of Occupational and Environmental Medicine, University of California at San Francisco; **Francisco Talavera, PharmD, PhD**, Senior Pharmacy Editor, Pharmacy, eMedicine; **Neil A Busis, MD**, Chief, Clinical Associate Professor, Department of Medicine, Division of Neurology, University of Pittsburgh Medical Center - Shadyside; **Selim R Benbadis, MD**, Director of Comprehensive Epilepsy Program, Associate Professor, Departments of Neurology and Neurosurgery, University of South Florida, Tampa General Hospital; and **Nicholas Lorenzo, MD**, eMedicine Chief Publishing Officer, Chief Editor, eMedicine Neurology; Consulting Staff, Neurology Specialists and Consultants

INTRODUCTION

Background: Organophosphates (OPs) are chemical substances originally produced by the reaction of alcohols and phosphoric acid. In the 1930s they were used as insecticides, but the German military developed these substances as neurotoxins in World War II. They function as cholinesterase inhibitors, thereby affecting neuromuscular transmission.

Organophosphate insecticides, such as diazinon, disulfoton, azinphos-methyl, and fonofos, are used widely in agriculture and in household applications as pesticides. Over 25,000 brands of pesticides are available in the United States, and their use is monitored by the Environmental Protection Agency (EPA). Diazinon has been sold

in the United States for 48 years. 14.7 million pounds are sold annually, and it is the most widely used ingredient in lawn and garden sprays in the United States. It is found under the brand names Real Kill, Ortho, and Spectracide.

The EPA reached an agreement with the pesticide industry to end the production of diazinon by March 2001 for indoor use and June 2003 for lawn and garden use. Chlorpyrifos (Dursban) was involved in a negotiated phaseout in June 2000. These phaseouts resulted from recognition of the special risk that these substances posed for children. Four percent of patients presenting to poison control centers report pesticide exposure. Of those patients, 34% are children younger than 6 years.

Toxic nerve agents used by the military are often of the organophosphate group; an example is sarin, the nerve gas used in a terrorist action in Tokyo in 1995. In anticipation of military use of OP neurotoxins during the Gulf War, the US military was given prophylactic agents which some believe caused some of the symptoms of Gulf War syndrome.

With the emergence of the West Nile virus in the northeastern United States, programs of spraying have been implemented in large urban areas, in particular New York's Central Park.

Controversy exists regarding the long-term effects of exposure to low levels of potentially neurotoxic substances.

Therapeutic uses of organophosphates

Several organophosphate agents are being tried therapeutically. Cholinesterase inhibition, which in large doses makes these agents effective pesticides, also may be useful in other doses for treating dementia. Metrifonate has been used to treat schistosomiasis and is undergoing trials for the treatment of primary degenerative dementia.

The organophosphates pyridostigmine and physostigmine are carbamate anticholinesterases that have been used for many years for the treatment of myasthenia gravis. Although the short-duration anticholinesterases are generally safe, reports of their abuse are associated with a picture similar to pesticide intoxication.

One of the author's patients had been diagnosed erroneously as a myasthenic. Long-term "therapeutic" doses of physostigmine chemically altered her neuromuscular junctions to the point where she had to be slowly weaned from the drug.

Sung and others have reported on the ability of these substances to induce nicotinic receptor modulation. This explains the action of these drugs and may result in development of more effective agents.

Historic and new uses of organophosphates

The first organophosphate was synthesized in 1850. Physostigmine was used to treat glaucoma in the 1870s. By the 1930s, synthetic cholinesterase inhibitors were being used for skeletal muscle and autonomic disorders. Some organophosphates

Myasthenia Gravis

Organic Solvents

Toxic Neuropathy

Continuing Education

CME available for this topic. Click here to take this CME.

Patient Education

Click here for patient education.

were tried in the treatment of parkinsonism.

In 1986, testing began for tacrine, the first cholinesterase inhibitor to be tried for Alzheimer disease; it was released for clinical use in 1993. The blood-brain barrier has been the limiting factor in developing a cholinesterase inhibitor for use in dementia. A new drug, rivastigmine, is now available. Reported adverse effects are nausea and vomiting, with resultant weight loss because of the increase in cholinergic activity. It has been shown to be useful in mild to moderately severe Alzheimer disease.

Recently, pyridostigmine has been tried for the fatigue of postpolio syndrome. Unfortunately, the study showed no benefit.

Pathophysiology: The mechanism of action, on both target and nontarget species, is irreversible inhibition of acetylcholinesterase (AchE). Acetylcholinesterase is found in red blood cells and in nicotinic and muscarinic receptors in nerve, muscle, and gray matter of the brain. Plasma acetylcholinesterase is found in CNS white matter, pancreas, and heart. It is a hepatic acute phase protein that often is decreased in liver dysfunction, malnutrition, neoplastic disease, pregnancy, and infectious processes as well as in narcotic or cocaine use. Decrease in plasma cholinesterase results in a decrease of cholinesterase activity in the central, parasympathetic, and sympathetic nervous systems.

Organophosphates phosphorylate the serine hydroxyl group at the site of action of acetylcholine. They bind irreversibly, deactivating the esterase and resulting in accumulation of acetylcholine at the endplate. Accumulation of acetylcholine at the neuromuscular junction causes persistent depolarization of skeletal muscle, resulting in weakness and fasciculations. In the central nervous system, neural transmission is disrupted. If this block is not reversed by a strong nucleophile such as pralidoxime (2-PAM) within 24 hours, large amounts of acetylcholinesterase are destroyed. RBC cholinesterase levels rise slowly; about 0.5-1% a day.

Delayed neurotoxicity

Delayed neurotoxicity is produced by certain organophosphorus esters classified as axonopathic. Few of the thousands of organophosphorus agents in the market have been associated with delayed onset of neuropathy. In those that produce neuropathy, effects may result from a single large dose or cumulative doses. Organophosphorus ester-induced delayed neuropathy (OPIDN) takes at least 10 days to develop following a single acute exposure. The effects of cumulative doses occur over a period of weeks following exposure.

Pathologic examination reveals central-peripheral distal axonopathy. Typically, the spinal cord tracts and distal axons of the lower extremities are involved more than the upper extremities. Primary axonopathy is accompanied by secondary demyelination. Sensory and motor fibers are involved. Interestingly, this late toxicity is not a result of acetylcholinesterase inhibition but rather a result of phosphorylation of a receptor protein, neurotoxic esterase, also called neuropathy target esterase (NTE).

Lotti et al described a second step, an "aging" of the phosphoryl-enzyme complex, that is required to produce the neurotoxic effect. Not all organophosphates cause

delayed neuropathy. An in vitro test measuring the catalytic activity of this neuron-specific enolase (ie, NTE) may be able to determine the risk of development of delayed neuropathy. Studies in hens given single doses of diazinon or triorthocresyl phosphate (TOCP), showed a "dying back" type of lesion that developed in hens exposed to TOCP but not those exposed to diazinon. Peripheral nerves were affected, and researchers noted moderately severe to marked degeneration of the folia of the cerebellum, the medulla, and spinal cord (the dorsolateral and dorsal columns). TOCP is not a cholinesterase inhibitor.

Frequency:

- **In the US:** In 1983, the rate of mortality from nonintentional pesticide poisoning was 2.7 per 10 million men and 0.5 per 10 million women. Generally, about 20,000 cases of organophosphate intoxication are reported yearly. About 2.3-2.6 per 10 million of the cases represent suicidal ingestion.

  In 1998, American Association of Poison Control Centers reported 16,392 exposures to organophosphates, with 11 reported deaths.

  The true number of exposures is likely to be underestimated. Most cases of cumulative exposure in agricultural workers go unreported.

- **Internationally:** Estimating the number of individuals exposed to organophosphates internationally is virtually impossible. Many agents considered too toxic to market in the United States still may be available in developing nations. Thirty percent of the pesticides exported from the United States are banned for use in the United States. Awareness of the dangers of pesticides is less in developing countries. The number of children exposed is likely to be greater in developing countries where children are expected to work on the family farm or may be hired out as laborers.

  The use of pesticides as agents of suicide is far more common in developing nations and may represent up to 99% of deaths by suicide.

Mortality/Morbidity: Mortality rate is generally low in patients treated promptly. Morbidity involves the late onset of neuropathy and tremor, and in large doses, convulsions and delirium. Other late effects are less expected. Compston et al reported reduced bone formation after exposure to organophosphates in 80 male agricultural workers. The mechanism of action was thought to be inhibition of acetylcholinesterase in bone matrix. Acetylcholinesterase is expressed by osteoblasts; it is present along cement lines and in osteoid. The author believes that acetylcholinesterase may have a role in the regulation of cell-matrix interactions and in the coupling of bone resorption and formation.

Frequently, the cumulative effects of low doses of organophosphates are neuropsychological. A joint report by the UK Royal College of Physicians and Psychiatrists concluded that a wide range of often-severe symptoms such as excessive fatigue, poor concentration, and suicidal thoughts are reported more frequently in populations exposed repeatedly. Exposed individuals often have a chronic flulike state that improves when exposure ceases. A patient the author saw 3 years after exposure to a single high dose of diazinon was left with significant cognitive impairment and episodes of generalized muscle hypertonia, initially

thought to be seizural. Chronic neuropsychological effects have been seen in 4-9% of patients exposed in occupation-related use.

Race: No particular racial susceptibility to organophosphate toxicity has been noted, but the reported incidence is 3-fold greater in African Americans. This may be a result of the predominance of African Americans in the at-risk population.

Menegon et al studied the possibility of genetic predisposition in patients who developed Parkinson disease after pesticide exposure. Glutathione transferase polymorphism was investigated. Glutathione transferase polymorphism 1 (*GSTP1*) genotypes appeared to be associated with the risk.

Studies by Bhatt et al may confirm the existence of genetic susceptibility. The risk of developing Parkinson disease after long-term pesticide exposure has been reported. Bhatt et al reported 5 cases of acute and reversible parkinsonism due to organophosphate pesticide exposure in India. One patient was a 31-year-old woman who ingested an organophosphate pesticide in a suicide attempt. The other 4 were exposed following household use of pesticides. Typical features of parkinsonism developed in all cases; however, the patients did not respond to levodopa-carbidopa administration. All patients improved when they were removed from the source of the toxin. Surprisingly, atropine, which is used to provide protection against the effect of organophosphates, was used to treat parkinsonism prior to the development of more effective agents.

Sex: Most cases of exposure involve agricultural workers or those involved in pest control; therefore, most reported cases are males.

- Susceptibility apparently is not increased inherently among males or females.
- Inhibition of RBC cholinesterase activity is greater in females than in males.

Age: Age does not appear to be a significant factor, although children exposed to pesticides may absorb relatively more chemical with respect to surface area. Children are also more likely to be exposed to pesticides used in lawn care in the course of play. Exposure to vaporized pesticide in the air, dermal exposure, and placing of pesticide-covered fingers in the mouth increase the routes of exposure.

History: Typically the patient with acute toxic effects of exposure reports being involved in agricultural spraying of crops or the use of pesticides in an enclosed space. Children become ill after playing in areas that have been treated. In the United States, suicidal ingestion is unusual but accidental ingestion by children may result in acute effects. The antihelminthic trichlorfon is used infrequently but may produce symptoms.

- Acute effects
    - Onset of symptoms occurs within hours of exposure. The acronym SLUDGE is used to describe the muscarinic manifestations of salivation, lacrimation, urination, defecation, GI distress, and emesis.

- Signs and symptoms of mild to moderately severe toxicity include tightness in the chest, wheezing, increased sweating, salivation, and lacrimation, as well as GI effects including nausea, vomiting, cramps, watery diarrhea, and involuntary defecation/urination.
- Pupils are constricted.
- Patients are anxious, restless, emotionally labile, and confused; they typically have insomnia and headache.
- Speech may be slurred and the patient may have ataxia, tremor, muscle weakness with cramping, and fasciculations.
- Seizures may occur secondary to anoxia.
- Death in organophosphate toxicity usually results from cardiac or respiratory failure.

- Delayed effects
  - Organophosphorus ester-induced delayed neuropathy takes at least 10 days to develop following a single acute exposure. The effects of cumulative doses occur over a period of weeks following exposure.
  - Cramping, tingling, ataxia, and weakness in the lower extremities, progressing to generalized weakness, may be seen in severe cases. Occasionally, a picture resembling amyotrophic lateral sclerosis may be seen in long-term exposure.

- Himuro et al described neuropathologic changes seen in a 51-year-old man exposed to the nerve gas sarin in a terrorist attack in Tokyo in 1995. He died 15 months after exposure. He was in cardiopulmonary arrest when seen in the emergency room and remained on a ventilator during hospitalization. He was found to have severe sensory and motor fiber loss in the sampled peripheral nerves. Myelinated fibers in the white matter of the spinal cord were totally lost except for well-preserved posterior columns. Brain changes were described as being consistent with hypoxic-ischemic encephalopathy.

- Tricresyl phosphate (TCP), in an isomeric combination, was involved in the notorious "ginger jake paralysis," which affected about 50,000 people in the United States in the 1930s and has caused outbreaks in India and South Africa. Senenayake and Jeyaratnam reported a group of over 20 Sri Lankan women affected by neuropathy associated with the intake of gingili oil contaminated with TCP. The occurrence of neuropathic complaints, 2-4 weeks after menarche, was the result of traditional ingestion of raw eggs and gingili oil (made from a type of sesame seed) to strengthen a woman after her first menstruation or in the case of 3 Moslem women, to strengthen them after childbirth. Paralysis involved distal limb muscles. Electrodiagnostic studies confirmed an axonal polyneuropathy.

Physical: The physical features of short-term and long-term exposure are detailed in History.

- In mild exposure, the picture is that of acetylcholine overload. The patient shows restlessness, has very active bowel sounds, and may have diarrhea and frequent urination.

- In more severe exposure, patients may exhibit muscle twitching and cramping, hypertension, and tachycardia, with an abdominal examination consistent with cramping and watery diarrhea. The patient is usually confused but may be drowsy.

- In more severe exposure, the patient may need ventilatory support with active pulmonary toilet because of respiratory failure and excessive secretions.

Causes: Job-related exposure to organophosphates is the most common cause of toxicity, particularly when care is not taken to use personal protective equipment. Domestic exposure occurs when spraying takes place in an enclosed, unventilated space or skin is exposed during application of a pesticide.

	DIFFERENTIALS	Section 4 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Acute Inflammatory Demyelinating Polyradiculoneuropathy
Assessment of Neuromuscular Transmission
Chronic Inflammatory Demyelinating Polyradiculoneuropathy
Diabetic Neuropathy
Essential Tremor
HIV-1 Associated Distal Painful Sensorimotor Polyneuropathy
HIV-1 Associated Multiple Mononeuropathies
HIV-1 Associated Neuromuscular Complications (Overview)
Myasthenia Gravis
Organic Solvents
Toxic Neuropathy

	WORKUP	Section 5 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Lab Studies:

- In the acute care setting, laboratory studies should include glucose, BUN, electrolytes, prothrombin time, liver function studies, and cholinesterase measurements.

- Levels of plasma and/or RBC cholinesterase enzyme may be measured by any of several existing methods. Most frequently used, because it is most readily available, is the test for plasma (or pseudo) cholinesterase. Because this can be affected by other disorders, it does not confirm the diagnosis. Mild intoxication is diagnosed when RBC cholinesterase inhibition is less than 50% of normal.

    - Depression of this value by 25% or more is confirmatory; this test may be used to follow progress.

- Workers exposed to organophosphates used in agriculture should have a baseline level recorded.

Imaging Studies:

- The only imaging study that may be useful in acute management is a chest x-ray because of the danger of aspiration pneumonia in a confused patient with vomiting and compromised respiration.

Other Tests:

- Electrocardiography should be done on admission, since many patients develop cardiac irregularities following acute exposure.
- Electrophysiologic studies
  - Acute organophosphate toxicity producing weakness is due to sustained endplate depolarization. In vivo microelectrode studies reported by Maselli and Soliven demonstrated no reduction in the amplitude of miniature endplate potentials or of the quantal content of the endplate potentials. Repetitive stimulation produced a decremental response as the endplate was "flooded" with acetylcholine.
  - Rutchik and Rutkove found a temperature-dependent response; cooling to 32°C produced a normal-amplitude compound action potential (CMAP). A smaller spontaneous repetitive response was elicited in a man with organophosphate intoxication. Warming the limb to 39°C caused these responses to decrease in amplitude; the authors likened the effect to that seen in myasthenia gravis.
  - Singh et al examined the phrenic nerve conduction of 29 patients with organophosphate toxicity admitted to the hospital in 1997, 14 of whom required mechanical ventilation. They found that reduction in CMAP correlated with need for ventilatory assistance. By following patients with daily studies, they were able to predict successful weaning.
- Neuropsychological testing: Workers exposed over a long period to pesticides have been reported to manifest irritability, fatigue, headache, and difficulties with memory and concentration.
- Evidence of neuropsychological abnormalities has been found in 4-9% of those who have had long-term exposure (Eskanazi and Maizlish; Tarter et al; Rosenstock et al)

Histologic Findings: Nerve biopsy in late-onset neuropathy reveals a primary axonopathy with secondary demyelination. CNS myelin may be lost as well.

	TREATMENT	Section 6 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Medical Care: The patient exposed to organophosphates often arrives at the hospital with cutaneous contamination. The clothing should be removed and discarded. All traces of residue must be removed by careful washing with alkaline soap or bleach solution.

- Laboratory studies should be drawn and a baseline ECG done.
- Patients who have had a high level of exposure and are obtunded should be intubated; those having

seizures or severe spasms should be given diazepam.

- Volume depletion may be a problem if the patient is having diarrhea. Intravenous infusion with 5% dextrose in water should be started.

Surgical Care: Surgical care such as tracheotomy and ventilatory assistance generally is not needed unless toxic effects are severe. In late-onset neuropathy, phrenic nerve function may be compromised and the patient may need ventilatory assistance.

Consultations: Consultation should be sought from pulmonary medicine, neurology, and if possible, psychiatry. An agitated patient requiring intubation in the acute phase of treatment can be difficult to control, as sedatives may worsen the condition.

Diet:

- Feeding the patient should be avoided until the patient's condition is stabilized.
- During acute intoxication, vomiting, diarrhea, and involuntary urination may occur.
- The patient should be hydrated intravenously.

Activity:

- Patients in the acute phase of organophosphate toxicity may be agitated and should be kept in a quiet environment. As weakness and respiratory difficulties resolve, normal physical activity can resume.
- The patient should be monitored closely during the first 24-48 hours.
- The patient may respond initially to therapy and then become confused or agitated, requiring repeat doses of medication.

	MEDICATION	Section 7 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Atropine was used as the sole treatment until oximes were developed; it is still used as the sole treatment in developing countries where oximes are not available. In the United States, oximes are used in mild cases; in more severe cases oximes are augmented by the use of atropine.

In cases of oral ingestion, activated charcoal in suspension may be used if the patient is seen within 30 minutes of ingestion.

Drug Category: *Antidotes* -- These agents reactivate cholinesterases inactivated by phosphorylation due to exposure to organophosphates.

	Pralidoxime chloride (Protopam, 2-PAM chloride) -- Strong nucleophilic agent that reactivates cholinesterase by reversing phosphorylation of serine hydroxyl group at active site of receptor membrane.

Drug Name	Should be used within first 12-24 h and may need to be repeated over 2- to 3-week period. One patient in India, who ingested OPs in suicide attempt, required 92 g of pralidoxime over 23-d period. Effective against OP that is not irreversibly bound. Metabolized in liver and excreted in kidney. Early treatment most effective. Half-life 74-77 min. Not effective against carbamates. Should be used in severe OP toxicity.
Adult Dose	When given with atropine, atropine is given first Atropine sulfate: 1-5 mg IV after cholinesterase levels measured; may repeat q10-30min until patient fully atropinized (ie, experiencing dry mouth, tachycardia, clearing of tracheobronchial secretions, dilated pupils) Pralidoxime: 1 g IV over 15-30 min when patient has fasciculations, muscle weakness, or respiratory depression on examination; may be repeated q8-12h for up to 3 doses
Pediatric Dose	25-50 mg/kg IV given as 5% solution in isotonic saline; repeat in 12 h if symptoms persist or recur
Contraindications	Documented hypersensitivity
Interactions	Potentiates action of barbiturates; antagonism with neostigmine, pyridostigmine, and edrophonium; morphine, theophylline, aminophylline, succinylcholine, reserpine, and phenothiazines can worsen condition of patients poisoned by OP insecticides or nerve agents (do not administer)
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Rapid injection can cause tachycardia, laryngospasm, muscle rigidity, pain at injection site, blurred vision, diplopia, impaired accommodation, dizziness, drowsiness, nausea, tachycardia, hypertension, and hyperventilation; can precipitate myasthenia crisis in patients with myasthenia gravis, and muscle rigidity in normal volunteers; decrease in renal function increases drug levels in blood because 2-PAM excreted in urine; can produce transient elevation in CPK; 1 of 6 patients have elevation in SGOT and/or SGPT

Drug Category: *Anticholinergic agents* -- These agents are used to reduce the clinical manifestations of organophosphate toxicity.

Drug Name	Atropine (I-Tropine) -- Antagonizes ACh at muscarinic receptor, leaving nicotinic receptors unaffected. Continue administration until excess muscarinic symptoms improve, which can be gauged by increased ease of breathing in conscious patient or improvement in ease of ventilation of intubated patient.
	1-2 mg/dose q10-20min to effect, then q1-4h for 24 h;

Adult Dose	not to exceed 50 mg in first 24 h (or 2 g over several days if intoxication severe)
Pediatric Dose	0.02-0.05 mg/kg IV q10-20 min to effect, then q1-4h for at least 24 h
Contraindications	Documented hypersensitivity; thyrotoxicosis; narrow-angle glaucoma; tachycardia
Interactions	Other anticholinergics have additive effects; may increase pharmacologic effects of atenolol and digoxin; may decrease antipsychotic effects of phenothiazines; TCAs with anticholinergic activity may increase effects
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in Down syndrome and/or children with brain damage to prevent hyperreactive response; caution also in coronary heart disease, tachycardia, congestive heart failure, cardiac arrhythmias, hypertension, peritonitis, ulcerative colitis, hepatic disease, and hiatal hernia with reflux esophagitis; in prostatic hypertrophy or prostatism, patients can have dysuria and may require catheterization

Further Inpatient Care:

- Following treatment of the acute manifestations of organophosphate poisoning, patients may develop tremor, cognitive deficits, and general debility; they may need treatment of these secondary consequences of organophosphate toxicity. In the case of the patient exposed to large amounts of diazinon, the effects initially were thought to be seizures but were in fact related to generalized nervous system hyperexcitability, which the author treated with Zanaflex.

Further Outpatient Care:

- Generally, after the treatment of acute effects of organophosphate exposure, no additional treatment is needed. Occasionally, the patient has residual neurophysiologic and neuropsychological sequelae.
- Patients exposed to an agent suspected of producing neuropathy require monitoring and electrodiagnostic studies several weeks following acute toxicity.
- Neuropsychological assessment on a periodic basis is recommended for workers with long-term exposure.
- Testing should be done for patients with complaints of memory problems and cognitive deficits.

In/Out Patient Meds:

- Generally, no medications are prescribed for the patient at discharge.

Transfer:

- Transfer to a rehabilitation facility may be indicated for the patient who develops late neuropathic sequelae.

Deterrence/Prevention:

- Use of pesticides in enclosed spaces generally results in exposure to organophosphates. Use of proper ventilation and avoidance of cutaneous exposure reduces toxic events. Many of the more toxic substances are being phased out of production. Carbamate pesticides, for example, while not totally benign, cause a less severe type of toxicity. The carbamates are cholinesterase inhibitors with a blockade time of about 6 hours. They do not cross the blood-brain barrier well and affect primarily the peripheral receptors.

- Care must be taken by those who use organophosphate pesticides commercially (eg, crop dusters, farmers); a healthy respect for the substances will help reduce cases of acute toxicity.

- Children should be kept from areas where pesticides have been applied.

Complications:

- Complications generally are seen during the period of hospitalization and involve respiratory difficulty, requiring intubation and ventilatory assistance. Seizures occurring during the acute phase should be treated with diazepam.

Prognosis:

- Promptly treated organophosphate toxicity carries a favorable prognosis.

- Individuals with long-term exposure need to be monitored for the late complication of neuropathy and development of cognitive abnormalities.

Patient Education:

- Pesticides can be dangerous substances if used improperly. They must be kept in a safe place and away from children. People using pesticides should be educated in the fact that the chemicals can enter the body by several routes and to use gloves, protective clothing, and even respiratory protection. After cutaneous exposure, immediate washing is a must.

- Patients exposed to pesticides at home should be cautious concerning the potential for repeat exposure. Individuals need to have proper ventilation and to use personal protective equipment such as plastic gloves and clothing that can be removed and laundered immediately after spraying is completed.

- Employers are required to provide protective equipment and to instruct their workers to avoid undue exposure by not applying pesticides downwind on a windy day.

	MISCELLANEOUS	Section 9 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Medical/Legal Pitfalls:

- The patient presenting acutely in an agitated state may not be able to give a clear history of what happened. The wheezing, tightness in the chest, and weakness may simulate an asthmatic attack. If possible, the container of the substance to which the patient was exposed should be brought to the hospital. Treatment with atropine and pralidoxime must be initiated immediately after the condition is diagnosed.

- The patient's response to the initial treatment may give a false sense of security; therefore, the patient should not be discharged until the effect of the organophosphate clearly has been totally reversed.

- Since many people susceptible to organophosphate toxicity are in work-related situations, workmen's compensation issues may arise.

- Many highly toxic pesticides have been removed from the market. However, some of these may be still in use.

- Failure to arrange for careful follow-up to monitor late complications can result in a possible medicolegal action.

Special Concerns:

- All toxic substances should be stored out of the reach of children.

- Exposure during pregnancy should be avoided.

- Of interest is the use of anticholinesterases in the elderly for the treatment of dementia. The adverse effects of these substances are essentially the same as those seen in pesticide toxicity but they are less severe.

	PICTURES	Section 10 of 11 [Back Top Next]
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

Caption: Picture 1. Chemical Terrorism Agents and Syndromes. Signs and symptoms. Chart courtesy of North Carolina Statewide Program for Infection Control and Epidemiology (SPICE), copyright University of North Carolina at Chapel Hill, www.unc.edu/depts/spice/chemical.html.

Picture Type: Image

	BIBLIOGRAPHY	Section 11 of 11 [Back Top
Author Information Introduction Clinical Differentials Workup Treatment Medication Follow-up Miscellaneous Pictures Bibliography		

- Bhatt MH, Elias MA, Mankodi AK: Acute and reversible parkinsonism due to organophosphate pesticide intoxication: five cases . Neurology 1999 Apr 22; 52(7): 1467-71[Medline].
- Compston JE, Vedi S, Stephen AB: Reduced bone formation after exposure to organophosphates . Lancet 1999 Nov 20; 354(9192): 1791-2[Medline].
- Eskanazi B, Maizlish NA: Effects of occupational exposure to chemicals on neurobehavioral functioning. Medical Neuropsychology 1988.
- Feldman RG: Organophosphates. Occupational and Environmental Neurotoxicology 1998; Lippincott-Raven.

- Himuro K, Murayama S, Nishiyama K: Distal sensory axonopathy after sarin intoxication. Neurology 1998 Oct; 51(4): 1195-7[Medline].
- Lotti M, Becker CE, Aminoff MJ: Organophosphate polyneuropathy: pathogenesis and prevention. Neurology 1984 May; 34(5): 658-62[Medline].
- Ludomirsky A, Klein HO, Sarelli P: Q-T prolongation and polymorphous ("torsade de pointes") ventricular arrhythmias associated with organophosphorus insecticide poisoning. Am J Cardiol 1982 May; 49(7): 1654-8[Medline].
- Maddy KT, Edminston S, Richmond R: Illness, injuries, and deaths from pesticide exposures in California 1949-1988. Rev. Environ Contam Toxicol 1990; 114: 58-123.
- Morgan JP, Penovich P: Jamaica ginger paralysis. Forty-seven-year follow-up. Arch Neurol 1978 Aug; 35(8): 530-2[Medline].
- Rosenstock L, Keifer M, Daniell WE: Chronic central nervous system effects of acute organophosphate pesticide intoxication. The Pesticide Health Effects Study Group. Lancet 1991 Jul 27; 338(8761): 223-7[Medline].
- Rutchik JS, Rutkove SB: Effect of temperature on motor responses in organophosphate intoxication. Muscle Nerve 1998 Jul; 21(7): 958-60[Medline].
- Savage EP, Keefe TJ, Mounce LM: Chronic neurological sequelae of acute organophosphate pesticide poisoning. Arch Environ Health 1988 Jan-Feb; 43(1): 38-45[Medline].
- Senanayake N, Jeyaratnam J: Toxic polyneuropathy due to gingili oil contaminated with tri-cresyl phosphate affecting adolescent girls in Sri Lanka . Lancet 1981 Jan 10; 1(8211): 88-9[Medline].
- Senanayake N, Karalliede L: Neurotoxic effects of organophosphorus insecticides. N Engl J Med 1987; 316: 761-763.
- Singh G, Sidhu UP, Mahajan R: Phrenic nerve conduction studies in acute organophosphate poisoning. Muscle Nerve 2000 Apr; 23(4): 627-32[Medline].
- Sung JJ, Kim SJ, Lee HB: Anticholinesterase induces nicotinic receptor modulation. Muscle Nerve 1998 Sep; 21(9): 1135-44[Medline].
- Taylor P: Development of acetylcholinesterase inhibitors in the therapy of Alzheimer's disease. Neurology 1998; 51(Suppl 1): S30-S35.
- Trojan DA, Collet JP, Shapiro S: A multicenter, randomized, double-blinded trial of pyridostigmine in postpolio syndrome. Neurology 1999 Oct 12; 53(6): 1225-33[Medline].
- Tune LE, Damlouji NF, Holland A: Association of postoperative delirium with raised serum levels of anticholinergic drugs. Lancet 1981 Sep 26; 2(8248): 651-3[Medline].